Incompatibility in Prescriptions

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Incompatibility in Prescriptions

And How to Avoid It

TO WHICH IS ADDED

A Dictionary of Incompatibilities

BY

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SOME TIME EXAMINER TO THE PHARMACEUTICAL SOCIETY OF GREAT BRITAIN

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"*Multa cadunt inter calicem supremaque labia*"

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PREFACE

THE time devoted to pharmacy and chemistry in the medical curriculum is necessarily short, and the student is generally launched into practice with a comparatively scant knowledge of how to write any but the most ordinary prescriptions. References to incompatibility of ingredients as given in textbooks usually take the form of tables, difficult to commit to memory because of their purely tabular nature. Much of the literature on the subject, moreover, deals with it from the pharmacist's point of view only. It is intended in these pages to study the subject of incompatibility in a systematic manner, illustrating with examples the various difficulties most likely to be met with by the physician in ordinary practice.

This book originally appeared in 1915 as a 32-page pamphlet. To all appearances it filled a want, and to meet the demand it was reprinted in 1916 and again in 1921. The original edition being again exhausted, a second edition, carefully revised, was issued in 1924, and reprinted in 1925. Only a very few copies of this 1925 reprint now remain unsold, and a further edition is called for.

Opportunity has therefore been taken of thoroughly revising the entire work, and of adding for reference purposes a complete Dictionary of Incompatibilities. It is now possible to ascertain with a minimum of trouble the exact difficulties to be encountered in dispensing any of the drugs now in common use. The work is practically a new book, and its size being increased to double that of the original pamphlet, it has been found desirable to bind it in cloth.

As far as possible, the incompatibilities described in the following pages have been verified experimentally; in the cases in which an authority is quoted, this has not been considered necessary. The writer desires to express his indebtedness to those authors, mentioned in the text, whose writings have furnished him with information.

T. S.

EDINBURGH, *July* 1929.

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PART I—GENERAL PRINCIPLES OF INCOMPATIBILITY

INCOMPATIBILITY has been defined as 'any unintentional change which notably interferes with the elegance, usefulness, or safety of a prescription.'[1] Such changes may belong to one of three classes: (1) chemical; (2) physical or pharmaceutical; (3) therapeutic.

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1. Chemical Incompatibility

Where the ingredients of a prescription interact chemically in the circumstances described above, that is, when such chemical action is not intentional, and interferes with the elegance, usefulness, or safety of the medicine, the prescription is said to be chemically incompatible. This may occur when:

(*a*) An insoluble compound is precipitated.
(*b*) Gas is evolved.
(*c*) An acid and an alkaline substance are mixed.
(*d*) One of the ingredients is decomposed.
(*e*) An alkaloid is precipitated.
(*f*) An undesirable compound is formed.

(*a*) **An Insoluble Compound is Precipitated.**—It is a recognized principle in chemistry that solutions of two soluble salts will invariably yield a precipitate when by mutual decomposition an insoluble salt can be formed, the tendency being always to revert to the more stable form. The salts most likely to be met with in prescribing that readily form such insoluble compounds are those of calcium, magnesium, iron, mercury, lead, zinc, and silver.

Calcium and Magnesium.—The soluble salts of calcium (chloride and bromide) give a precipitate with alkaline hydroxides, carbonates, sulphates, and phosphates. Aromatic spirit of ammonia is thus incompatible with calcium chloride.

[1] Walter G. Smith: *Incompatibility and Some of its Lessons* (1911).

The same is true of sodium sulphate in the following prescription:—

℞	Calcii chlorid. - - - -	gr. lxxx.
	Sodii sulph. - - - -	℥i.
	Syr. zingib. - - - -	℥i.
	Aq. cinnam. - - - -	ad ℥viii.

In this case a precipitate of calcium sulphate (plaster of Paris) is formed. Similarly any combination that would form calcium hydroxide, carbonate, or phosphate would be incompatible. Soluble oxalates also precipitate calcium salts.

Magnesium salts behave very similarly to those of calcium, except that they do not precipitate with bicarbonates or with ammonium carbonate. Magnesium sulphate (Epsom salts) gives a clear solution with sodium bicarbonate or with ammonium carbonate, but is precipitated by sodium phosphate. The following prescription is therefore incompatible:—

℞	Magnes. sulph. - - - -	℥vi.
	Sodii phosph. - - - -	℥vi.
	Aquam - - - - - -	ad ℥vi.

A thick flocculent precipitate of magnesium phosphate is formed.

Iron and Mercury.—The insoluble salts of iron are the carbonate, the hydroxide, and the phosphate; consequently, the soluble iron salts are incompatible with the soluble (*i.e.*, the alkaline) carbonates, hydroxides, and phosphates, and with preparations containing these, such as aromatic spirit of ammonia. Ferrous sulphate and sodium (or potassium) carbonate precipitate green ferrous carbonate, a reaction intentionally employed in making the mistura ferri composita of the B.P., or the well-known Blaud's pill.

The oxides and iodides of mercury are insoluble; soluble mercurials will therefore give a precipitate with soluble oxides and iodides, such as those of calcium or potassium. The calcium-mercury reaction is utilized in the pharmacopoeial 'black wash' and 'yellow wash,' mercurous and mercuric oxide respectively being precipitated. Potassium iodide and mercuric chloride throw out red mercuric iodide, which, however, is soluble in excess of the potassium salt, and is often intentionally prescribed in this form.

Lead, Zinc, Copper, and Silver.—Lead acetate and subacetate—the most commonly used salts of this metal—very readily precipitate, most of the lead salts being insoluble. Thus, any substance that on mixing will form lead oxide, carbonate, sulphate, chloride, bromide, sulphide, iodide, phosphate, tartrate, benzoate, citrate, salicylate, tannate, etc., cannot be mixed with either of these soluble lead salts. Alum and zinc sulphate are

examples. Any organic substance containing tannin, or any compound containing sulphur, is incompatible with lead acetate. Gum arabic is precipitated by lead subacetate. Mucilage, therefore, should not be prescribed along with it.

In some cases sulphur and lead acetate are purposely combined, as in certain hair lotions in which lead sulphide is the desired ingredient.

Zinc and copper salts are incompatible with alkaline hydroxides, carbonates, and phosphates; also with borax, insoluble zinc or copper compounds being formed.

The following lotion of zinc sulphide, which is a favourite with some skin specialists, is worthy of notice here :—

℞	Potass. sulphurat. - - -	℥ss.
	Zinci sulphat. - - - -	℥ss.
	Aq. rosæ - - - - -	℥iii.

In this case what is wanted is a suspension of insoluble zinc sulphide. When properly prepared (by dissolving the salts separately and filtering the potash solution into the zinc solution) a milky liquid containing freshly precipitated zinc sulphide is produced, and the liquid is free from odour of H_2S, and smells only of rose. The potassa sulphurata must be fresh; an old specimen will give no precipitate.

Silver salts are incompatible with chlorides, silver chloride being insoluble. For this reason only distilled water should be used in making solutions of silver nitrate. Similarly, common salt is useful to neutralize excess of silver nitrate applied to the eye or elsewhere. Silver nitrate is incompatible with alkaloidal hydrochlorides, such as those of morphine or cocaine; the nitrates of these alkaloids should be ordered in such a case.

In many cases a mixture which is chemically incompatible may be rendered quite presentable by the dispenser who understands the order of mixing the ingredients. For example :—

℞	Hydrarg. perchlor. - - - -	gr. ss.
	Ammon. carb. - - - -	gr. v.
	Potass. iodid. - - - -	gr. v.
	Aquam - - - - -	ad ℥i.

If added in the order given, the ammonium carbonate will precipitate the mercury; if, however, the perchloride and iodide be first dissolved, and the carbonate added to the solution, no precipitate will occur.

Tincture of perchloride of iron is precipitated by ammonia, as in spirit. ammon. aromat. But if the tincture be diluted with water and mucilage added to it, the subsequent addition of ammonia will not make the mixture inelegant.

(*b*) **Evolution of Gas.**—It is well known that when an acid stronger than carbonic acid is added to a solution of a carbonate or bicarbonate, the stronger acid forms a salt with the base, and CO_2 gas is liberated. This principle is made use of in the prescription of effervescent mixtures, in which the solution is prescribed in two separate bottles, containing respectively solutions of bicarbonate of potash or soda and citric acid in proper combining proportions. A dose from each bottle is mixed, and the resulting liquid drunk during effervescence. Again, the following prescription for calcium lactate is an example of an intentional combination of this character :—

℞	Calc. carb. præcip. - - -	ʒi.
	Acid. lactic., B.P. - - -	♏130.
	Aquam - - - -	ad ℥vi.

Here the calcium carbonate dissolves with effervescence in the lactic acid, but as the intention is to give calcium lactate in solution, and as the liquid is not bottled until effervescence has ceased, no harm is done by the evolution of gas.

Perhaps the most common instance of such incompatibility is the prescription of bismuth subnitrate or salicylate with sodium bicarbonate. These bismuth salts being acid, slow effervescence takes place, and the evolution of gas is sometimes sufficient to burst the bottle. Suitable dispensing may reduce this trouble to a minimum, but it is always advisable to prescribe bismuth *carbonate* only in conjunction with sodium bicarbonate.

Chalk mixture contains calcium carbonate, and the addition of an acid is inadmissible. It ought not therefore to be prescribed with bismuth subnitrate, or with dilute or aromatic sulphuric acid, for example.

Aromatic spirit of ammonia contains ammonium carbonate, and will effervesce with acid substances. In prescribing a cough mixture this incompatibility should be borne in mind. When such a mixture is to contain sodium bicarbonate, ammonium carbonate, or aromatic spirit of ammonia, then the prescriber must steer clear of syrup, oxymel, or vinegar of squill, syrup of lemon, vinegar of ipecacuanha, or any other acid preparation.

Liquid pepsin preparations invariably contain hydrochloric acid, and are therefore incompatible with sodium or potassium bicarbonates. Grey powder, which contains chalk, should not be prescribed with confection of sulphur, which contains potassium acid tartrate.

Other acid substances that ought never to be prescribed along with carbonates are: alum, glycerin of borax, liquor arsenici hydrochlor., spiritus aetheris nitrosi, etc.

In addition to the evolution of CO_2 from carbonates, other instances in which gas is liberated may be mentioned. The addition of hydrochloric acid to potassium chlorate gives rise to

chlorine gas, a reaction which is taken advantage of in preparing Gargarisma Chlori, B.P.C. Chlorine is also produced when potassium chlorate and alum are dissolved together.

Explosive Reactions.—Some space may here be devoted to the question of explosive reactions. An explosion is the result of a very sudden evolution of gas, and any incompatibility which in ordinary circumstances produces simple effervescence may under suitable conditions evolve gas with explosive violence. For example, a mixture containing bismuth subnitrate and sodium bicarbonate will, as already explained, effervesce, and if the bottle is kept in a cool place and only lightly corked nothing very serious may happen. But in a warm sickroom the reaction may be so violent as to burst the bottle, causing a severe shock to the patient's nerves, apart from the possibility of material damage.

Perhaps the most dangerous drug in this respect is potassium chlorate. Any reducing agent (see table on p. 12) is dangerously incompatible with it. The presence of potassium chlorate tablets in the same pocket as lucifer matches has been known to set the clothes on fire. The chlorate is occasionally combined with tannin and sugar for ear, nose, and throat troubles. Such a combination is liable to explode from friction. Compound liquorice powder contains sulphur and should not be combined with the chlorate. Sugar, saccharin, charcoal, astringent drugs containing tannin, antimony sulphide, etc., all form explosive compounds with it. Hypophosphites are particularly dangerous. The following solution, especially in a warm temperature (such as that of a sickroom, or when the bottle is carried in the pocket), is very liable to explosion :—

℞	Potass. chlorat. - - - -	℥iii.
	Tinct. ferri perchlor. - - -	℥ii.
	Glycerin - - - - -	℥ii.

Potassium permanganate is another dangerous substance. When ordered in pills it is best to leave the choice of excipient to the pharmacist and to combine no other drug with it, as all organic substances reduce the permanganate. The safest rule is never to prescribe it with anything except pure water.

Spirit of nitrous ether also has certain dangerous tendencies. With tannic acid it liberates gaseous compounds of nitrogen, sometimes slowly, sometimes very energetically. A mixture containing spirit of nitrous ether and almond mixture has been known to explode, probably as a result of the presence of tannin in the gum, one of the ingredients of the almond mixture. For the same reason the spirit should not be prescribed with astringent vegetable infusions such as buchu, uva ursi, etc.

Chromic acid is a powerful oxidizing agent, and in contact

with alcohol, glycerin, etc., at once explodes. Bichromates, in presence of mineral acids, behave similarly.

Hypophosphites are liable to explode when simply heated or triturated in a mortar. Picric acid is the basis of several military explosives. Nitroglycerin is safe in one per cent. alcoholic solution, but this solution when diluted deposits an oily substance which is highly explosive. Stronger solutions (5 and 10 per cent.) are not safe. Should a solution be spilled, some caustic potash solution should be poured over it to effect decomposition. (Nitroglycerin is thus incompatible with alkalis.) The chocolate tablets are quite safe as the nitroglycerin is in solution. The same applies to erythrol tetranitrate, which is also explosive.

Iodine forms explosive compounds with some essential oils. With ammonia it forms a very dangerous explosive, nitrogen iodide. An example of this is given at the end of this section.

Hydrogen peroxide should never be prescribed in combination. A bandage soaked in the peroxide is said to have ignited when dry.

The following table, compiled by G. W. Udale,[1] gives the more important oxidizing and reducing agents. All the substances given in the first list are incompatible with those in the second, and their combination should be carefully avoided.

Oxidizing Agents.	*Reducing Agents.*
Chlorates and hypochlorites.	Arsenious acid.
Chlorine; nitro-hydrochloric acid.	Cyanides.
Bromine and iodine.	Phosphorus; hypophosphites.
Bromates and iodates.	Sulphur, sulphides, sulphites, hyposulphites.
Chromates, bichromates, chromic acid.	Nitrites.
Nitrates and nitrites.	Oxalates.
Permanganates; peroxides (H_2O_2); persulphates.	Pyrogallol.
Lead and manganese dioxides.	Ferrous, mercurous, and stannous salts.
Silver oxides.	Iron and zinc powder.
Sulphuric acid (with organic matter).	Formaldehyde.
Ferric, mercuric, and cupric salts.	Organic bodies, including alcohol, glycerin, ethers, tannins, sugars, vegetable drugs, charcoal, cork, syrups, extracts, volatile and fixed oils, pyroxylin, creosote, etc.

One or two of the examples given by the same author are instructive:—

℞ Acid. nitro-hydrochl. dil. - - - ℥ss.
Tinct. cardam. co. - - - - ℥iss.

Likely to explode after an hour or two.

G. W. Udale: *British and Colonial Druggist*, Mar. 26, 1915.

℞ Acid. chromic.
Glycerin.
Alcohol - - - - āā p. aeq. ad ℥ss.
Very inflammable and explosive.

℞ Tinct. iodi - - - - - - ℥i.
Lin. camph. co. - - - - - - ℥iii.
Nitrogen iodide, a powerful explosive, is liable to be formed.

℞ Glycothymolin - - - - - ℥iss.
Liq. hydrog. perox. - - - - ℥iss.
Aquam - - - - - ad ℥xii.
A dangerously explosive combination.

(*c*) **Acids and Alkalis.**—The mixing of acid and alkaline liquids should as a rule be avoided. No prescriber would deliberately combine, say, hydrochloric acid with ammonia, but one is apt to forget at the moment of prescribing whether any particular preparation is acid or alkaline, and to combine such substances unwittingly. For example, liquor arsenicalis is alkaline and steel drops acid, yet one often sees these combined in a prescription—an obvious error. The simplest plan under this head will be to enumerate some of the more important alkaline and acid preparations, and leave prescribers to judge for themselves.

Alkaline Preparations.	*Acid Preparations.*
Liquor arsenicalis.	Mineral and organic acids.
Spirit. ammon. aromat.	Liquor arsenici hydrochlor.
Linim. camph. ammon.	Syrups of iron, etc., phosphate.
Lime water.	Syrups of lemon and squill.
Liquor bismuthi.	All the wines and vinegars.
Ammoniated tinctures.	Spiritus aetheris nitrosi.
Alkali salts.	Liquor ferri perchlor.
	Liquor pepticus.
	Linim. tereb. acet.

Such combinations as: linim. tereb. acet. and liq. ammon., acid. nitro-hydrochl. dil. and spir. ammon. arom., lime water and lactic acid, liquor pepticus and liquor bismuthi, etc., are therefore incompatible and should be carefully avoided.

One exception may be mentioned to this rule of 'acid *v.* alkali': Sodium bicarbonate and other alkalis may with all correctness be prescribed along with hydrocyanic acid. The alkaline cyanide formed has practically the same therapeutic action as hydrocyanic acid. (See also p. 16.)

(*d*) **Decomposition of the Ingredients.**—It is well-known in chemistry that salts of a weak acid are decomposed by a stronger acid. That is to say, the stronger acid has a greater affinity for the base, with which it readily combines, setting free the other acid. This happens when a mineral acid,

such as nitric or hydrochloric, is added to a benzoate, salicylate, or cinnamate. A solution of sodium salicylate or benzoate will, therefore, be decomposed by the addition of a mineral acid: salicylic or benzoic acid, which is only slightly soluble in water, is set free. Sometimes the liberated acid is diffusible in the mixture and easily shaken up, as is the cinnamic acid precipitate in the following mixture:—

℞	Calcii glycerophos. - - -	ʒii.
	Sodii cinnamatis - - -	gr. xx.
	Acid. phosph. dil. - - -	℥i.
	Glycerini - - - - -	℥i.
	Infus. aurant. co. - -	ad ℥vi.

It should be borne in mind in this connexion that caffeine citrate is readily dissociated in aqueous solution, citric acid being set free, and that this citric acid may act on a salicylate or a benzoate in the same manner as would a mineral acid. For example, the following combination gives a bulky precipitate of salicylic acid, which may be avoided by using half the amount of pure caffeine:—

℞	Caffein. cit. - - - -	gr. lxxx.
	Sodii salicyl. - - - -	gr. clx.
	Syr. tolut. - - - - -	℥i.
	Aq. chlorof. - - -	ad ℥viii.

Solutions of iodides are decomposed by certain mineral acids, iodine being set free. Potassium iodide is thus incompatible with dilute nitric or nitro-hydrochloric acid, or with tincture of ferric chloride, the liberated iodine forming a brown solution. Spirit of nitrous ether, when kept for any length of time, becomes acid and acts in the same way on potassium iodide. This action may be avoided by previous neutralization of the spirit by means of potassium carbonate, or by addition of a suitable quantity of ammonium carbonate to the prescription.

Acetyl-salicylic acid (aspirin) may decompose potassium iodide, and when the two are ordered in cachets the liberated iodine will combine with the starch contained in the envelope, forming an unsightly bluish-black compound.[1] Some essential oils, especially if long kept, have the power of decomposing potassium iodide.

On account of this liberation of iodine, potassium iodide should not be prescribed with paraldehyde. The same applies to ferric chloride, and the tincture should not be given with the iodide. Scale preparations of iron, however, such as ferri ammon. cit., are quite compatible with potassium iodide. In a mixture containing potassium iodide and ammonium chloride (according to Duncan[2]) the salts interact, liberating some acid,

[1] This reaction will not take place if both substances are reasonably pure.

[2] *British and Col. Druggist*, Mar. 31, 1911.

which breaks down into iodine and water. A yellow colour develops in the mixture, but this will not take place if the mixture is alkaline.

Another instance in which iodine is set free, though not immediately, is when potassium chlorate is prescribed with syrup of ferrous iodide. In this case the chlorate is gradually reduced to chloride, and iodine is liberated from the ferrous iodide. In a case quoted by W. G. Smith the iodine liberated in such a mixture caused the death of a child.

Glucosides are hydrolysed in presence of mineral acids or alkalis. Thus salicin is slowly changed into saligenin and glucose, and strophanthin is similarly decomposed.

Reference has already been made under the heading of explosives (see p. 11) to the decomposition of substances rich in oxygen.

Chloral hydrate is another substance that is readily decomposed. With carbonates or hydroxides of the alkalis or alkaline earths (potassium, sodium, ammonium, or magnesium) chloroform is set free, and a formate of the base is produced. With certain soluble salts, such as bromides and iodides, in presence of alcohol, an oily layer of chloral alcoholate is formed. It is therefore unwise to prescribe chloral hydrate and potassium bromide along with a tincture.

(*e*) **Precipitation of Alkaloids.**—As a general rule, alkaloids are insoluble in water, and can be held in solution only by addition of an acid, which forms a soluble salt. The addition of an alkali to such solution will neutralize the acid and throw out the alkaloid in an insoluble form. Ammonia, such as aromatic spirit of ammonia or ammoniacal tinctures, alkaline carbonates, etc., ought not therefore to be prescribed with alkaloidal solutions.[1] Strychnine is very slightly soluble in water (about 1 in 7000), and *if sufficient water be used to dissolve the precipitated strychnine* an alkali may be added with safety. But at least one ounce of water should be added for every 6 minims of liquor strychninae hydrochlor.—*i.e.*, ℥i of liq. strych. hydrochlor. requires a 10 ounce or 12 ounce mixture to keep the liberated strychnine in solution if alkali is present. In the following prescription the strychnine was thrown out and taken with the last dose, causing severe symptoms of strychnine poisoning :—

℞	Potass. bicarb. - - - -	℥v.
	Liq. strychninae - - -	℥iss.
	Infus. gent. co. - - -	ad ℥vi.

[1] Quinine, though precipitated by ammonia, is soluble in excess of that substance ; this fact is utilized in the preparation of ammoniated tincture of quinine. The alcohol in this tincture assists in holding the quinine in solution, and addition of water precipitates the alkaloid, as is well known. But there is no precipitation with aerated water, the CO_2 forming a soluble carbonate. The solution with aerated water is more palatable,

When arsenic is prescribed along with an alkaloid the liquor arsenici hydrochlor. should be used. A prescription containing liq. strych. and liq. arsenicalis has been known to cause the death of a patient.

An alkaloid may be prescribed with an effervescing mixture only if added to the acid portion.

Other substances that precipitate alkaloids are: tannic acid, iodine and iodides, bromides, salicylates, benzoates, mercuric chloride, picric acid. Acid. hydrocyan. dil. is said to form with morphine insoluble morphine cyanide, but our experiments do not confirm this.

Tannic acid is contained in most vegetable infusions and decoctions. Alkaloids should therefore never be prescribed with such. Infusion of quassia, it may be noted, contains no tannin, nor do infusions of calumba and chiretta. The following prescription is incompatible :—

℞	Quinin. sulph. - - - -	gr. xvi.
	Acid. sulph. dil. - - - -	ʒss.
	Infus. krameriae - -	ad ℥viii.

Iodine and *iodides* precipitate the alkaloid as insoluble hydriodide. For example, in the following mixture the nitric acid liberates iodine from the potassium iodide, and quinine hydriodide is thrown out :—

℞	Quinin. sulph. - - - -	gr. xxiv.
	Acid. nitric. dil. - - - -	♏xxx.
	Potass. iodid. - - - -	ʒii.
	Aquam - - - -	ad ℥vi.

When iodides or bromides are prescribed with strychnine the precipitation may take place so slowly as to be practically unnoticed, and the whole of the strychnine may be taken with the last dose.

Double iodides, such as Donovan's solution (liquor arsenii et hydrargyri iodidi) and Mayer's reagent (potassio-mercuric iodide), precipitate all alkaloids except caffeine and theobromine. It should also be remembered that in a mixture containing potassium iodide and liquor bismuthi, the double iodide of bismuth and potassium (Dragendorff's reagent) is formed, which precipitates most alkaloids. The following prescription is an example of precipitation by Mayer's reagent :—

℞	Hydrarg. perchlor. - - -	gr. i.
	Potass. iodid. - - - -	ʒii.
	Infus. calumb. - - -	ad ℥iii.

This mixture, according to Dunlop,[1] throws down a yellow precipitate consisting of double iodide of mercury and berberine.

[1] *Pharmaceutical Journal*, Jan. 27, 1912.

Dispensed with infusion of quassia, or compound infusion of gentian, both of which are free from alkaloids, it remains bright.

Alkaline *salicylates* and *benzoates* precipitate most alkaloids. The following prescription is therefore incompatible :—

℞	Quinin. sulph. - - - -	gr. xxiv.
	Sodii salicyl. - - - -	ʒi.
	Acid. sulph. dil. - - - -	♏xl.
	Aquam - - - -	ad ʒvi.

When, however, the acid is omitted and the *alkaline* ammoniated tincture is substituted for the quinine sulphate, a clear solution is obtained.

Mercuric chloride precipitates most alkaloids. *Picric acid* precipitates quinine, and is used as a test for the presence of quinine in the urine. *Borax* partially precipitates morphine and cocaine. *Boric acid*, however, does not, and may be prescribed with these alkaloids. *Sodium arsenate* precipitates strychnine and quinine.

(*f*) **Formation of an Undesirable Compound.**—The most familiar instance of this is the production of iron tannate (or 'ink') when salts of iron are mixed with any substance containing tannin. Nearly all vegetable drugs contain tannin: the exceptions are quassia, calumba, and chiretta, and these alone should be prescribed along with iron.

Ferric salts give with salicylates a deep purple colour of ferric salicylate. Suitably prescribed and properly dispensed, however, a mixture containing these ingredients is quite elegant. The following prescription has been recommended in cases of rheumatic sore throat :—

℞	Sodii salicylatis - - - -	ʒi.
	Liq. ferri perchlor. - - -	ʒss.
	Potass. bicarb. - - - -	ʒi.
	Aquam - - - -	ad ʒviii. Misce.

The iron must be mixed with the salicylate before the potash is added to either of them, otherwise an insoluble ferrous carbonate is formed and CO_2 is given off. The salicylate and the potash should each be dissolved in water: the salicylate solution is put in the bottle and the ferric chloride added to it, then the potash solution, and the bottle filled up with water. The result is a clear claret-coloured mixture, without a trace of deposit or effervescence.

Ferric chloride gives with acetates a blood-red colour due to the formation of ferric acetate. This, while therapeutically admissible and harmless (as in Basham's mixture, which contains tincture of perchloride of iron, acetic acid, and ammonium acetate), should nevertheless be borne in mind when the two are prescribed. A red colour of ferric meconate (also harmless)

is formed when ferric chloride and tincture of opium are combined in the same mixture. Ferric chloride also gives a violet colour with carbolic acid, and a deep red colour with phenazone (antipyrin).

Spirit of nitrous ether is another preparation that forms unexpected compounds. With phenazone it gives a brilliant green colour; with resorcin a dark red; with salicylates a yellow to red. Spirit of nitrous ether, especially after being kept for a time, contains free acid, and this fact has to be borne in mind when it is prescribed along with potassium iodide, for unless previously neutralized it will liberate iodine. Neutralization of the spirit tends to retard some of the other reactions already mentioned; but on the whole it is better to avoid such combinations altogether, and to prescribe the spirit in the simplest form possible. (See also *Explosive Reactions*, p. 11.)

Mercurials are another class of preparations that frequently give trouble in dispensing. Reference has been made to the insoluble precipitates formed in certain circumstances by salts of mercury. The tendency of mercurous salts (such as calomel) to be converted under certain conditions into the more poisonous mercuric salts should not be forgotten. Calomel and potassium bromide, for example, in presence of a trace of moisture, form a mercuric salt with precipitation of metallic mercury:—

$$Hg_2Cl_2 + 4KBr = (HgBr_2 2KBr) + 2KCl + Hg.$$

Potassium iodide has a somewhat analogous effect upon calomel. Calomel and phenazone (antipyrin) react to form corrosive sublimate, but as only about 10 per cent. of the calomel is thus converted, the matter is unimportant in the case of small doses. Sodium bicarbonate is also said to convert calomel into corrosive sublimate, but no toxic effects appear to have been observed from such a combination. In fact the process of conversion, if indeed it takes place at all, is a very slow one, and may be disregarded, especially as sodium bicarbonate is often a useful addition to calomel.

Tincture of iodine and calomel react with precipitation of mercuric iodide. Such a lotion has been used with success in the treatment of ringworm, calomel, 5 grains, stirred with tincture of iodine, one drachm, being rubbed to the parts.[1]

Mercurial applications, such as ointments, should be avoided in the case of patients taking an iodide, such as potassium iodide, or syrup of iodide of iron. Cases of this nature are discussed in the section dealing with therapeutic incompatibility.

To conclude this section on chemical incompatibility, a few special examples of incompatibility may be given.

Acetylsalicylic acid, or aspirin, is readily dissociated in presence of moisture into acetic and salicylic acids. It is there-

[1] Robertson: *B.M.J.*, June 16, 1923; Abstr. PRESCRIBER, Nov. 1923, p. 392.

fore best prescribed dry in cachets or tablets. Tablets that smell of acetic acid should not be used: they have become partly decomposed. Acetylsalicylic acid is decomposed by alkalies; carbonates cause effervescence. Though insoluble in water, it may be dissolved by means of sodium or potassium citrate, but it seems probable that such a solution consists of alkaline acetate and salicylate.

Some years ago a 'scare paragraph' went the round of the medical and pharmaceutical journals to the effect that aspirin formed a toxic compound with quinine. This has been shown to be untrue; indeed, quinine sulphate and acetylsalicylic acid may conveniently be prescribed together in a *mixture*, the acid causing the quinine to dissolve by forming soluble quinine acetylsalicylate. Powders containing quinine and aspirin, though to all appearances keeping fairly well, are likely to decompose after a time, liberating salicylic acid. Other points regarding aspirin will be found on pp. 14 and 21.

Adrenalin is incompatible with many drugs. It is very liable to oxidation, either by the air or by some oxidizing agent, and when oxidized is more or less inert. The acid in the official solution prevents oxidation; alkalis not only neutralize this acid, but themselves promote oxidation. Other oxidizing agents, such as iodine, chlorine, potassium permanganate, nitrites, peroxides, etc., are also incompatible with adrenalin. Ferric chloride hastens oxidation very rapidly, colouring the solution bright green (one of the tests for adrenalin). Traces of iron in any substance—even in the water or the glassware—will hasten oxidation and render the solution inert in a short time. The hydrochloric acid used in making the official solution must be free from iron. Formaldehyde is incompatible with adrenalin. Nitric and nitrohydrochloric acids act as oxidizing agents; other dilute mineral acids, if free from iron, are compatible with adrenalin. It is safest, however, *to prescribe adrenalin solution alone*, without any admixture.

Chloramine-T is decomposed by alcohol and by hydrogen peroxide. For the same reason it should not be combined with other antiseptics, but should be used alone in aqueous solution. As it attacks metals, it should not be used to sterilize instruments.

Gum acacia forms a thick precipitate with solution of lead subacetate (not with acetate), with ferric salts, with borax, and with alcohol and all spirituous preparations. It gives coloration with certain alkaloids, such as morphine and eserine, also with adrenalin. Acacia sometimes prevents precipitation, as in the case of alkaloids by tannic acid.

Hexamine (urotropin) is a drug requiring care in the matter

of combination. Sodium acid phosphate, if given at the same time, should be given separately and not in the same mixture. Powders containing hexamine and acetylsalicylic acid soon liquefy. Other combinations have also been found to be incompatible, and it is advisable always to order hexamine *per se*, and to give separately any other drugs that may be required at the same time.

Liquid extract of liquorice is incompatible with acids, the glycyrrhizin being precipitated. Glycyrrhizin is soluble in alkalis. Addition, however, of magnesium sulphate upsets the equilibrium, and a mixture containing magnes. sulph., extract glycrr. liq., and ammonia is most unsightly. When liquorice is used to mask the taste of quinine, no acid should be ordered; the quinine should be suspended in the mixture.

Mercurochrome, the new antiseptic, which is the sodium salt of dibromo-oxymercury-fluorescein, is incompatible with acids, which precipitate an insoluble mercury compound. It is also precipitated by cocaine, by novocaine, and by practically all the local anaesthetics.

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2. Physical or Pharmaceutical Incompatibility

It is difficult to draw a distinct line of demarcation between the two forms of incompatibility—chemical and physical. Many instances are actually on the border line, and cannot with certainty be relegated definitely to one or the other. But as a general rule one may class under the heading of physical or pharmaceutical incompatibility such cases as :—

(*a*) Insolubility.
(*b*) Immiscibility.
(*c*) Undesirable change of colour.
(*d*) Unsuitable consistence or excessive bulk.
(*e*) Molecular change.

(*a*) **Insolubility.**—The solvents usually employed in prescriptions are water, alcohol, glycerin, fixed oils, and occasionally ether and chloroform. Water is the solvent usually employed for mineral salts; alcohol for resinous substances and essential oils; glycerin comes midway between alcohol and water; fixed oils, ether, and chloroform are only occasionally employed as solvents for special substances.

The following general rules as to solubility in water will be found useful :—

Soluble in Water: All the ordinary salts of potassium, sodium, and ammonium. Most nitrates, chlorates,[1] acetates,

[1] Potassium chlorate is soluble 1 : 16 of water : solutions should contain not more than 30 grains to an ounce of water.

nitrites, bromides, chlorides, and iodides. Notable exceptions are silver chloride and bromide, mercurous chloride (calomel), bismuth oxynitrate (subnitrate), and the iodides of lead, bismuth, silver, and mercury.

Insoluble in Water: Carbonates, phosphates, oxides, hydroxides, sulphides, oxalates, *except* those of the alkalis.

Alkaloids as a rule are insoluble in water, but their salts are generally soluble, especially in an acid solution. Quinine sulphate, for example, requires the addition of dilute sulphuric acid, about one minim to each grain, to effect solution.

Lime (calcium hydroxide) is sparingly soluble in water, lime water being a saturated solution. The addition of sugar aids solution, as is seen in liquor calcis saccharatus. Zinc chloride is very soluble in water, but in dilute solutions a flocculent precipitate of zinc hydroxychloride is thrown down. The solution can readily be cleared by the addition of a few drops of diluted hydrochloric acid.

Carbolic acid is soluble in about 12 parts of water. The usual strength of carbolic lotion is 1 : 20, in which proportion the acid is easily soluble. For stronger solutions glycerin should be used as described below. Salicylic acid is only sparingly soluble in water (1 : 500). Boric acid is soluble about 1 : 30, the saturated solution generally employed as a lotion being about this strength. Tannic acid is freely soluble in water. Arsenious acid is soluble 1 : 100 of water, a solution of this strength being neutral and compatible with both acids and alkalis. Liquor arsenicalis is alkaline, and liquor arsenici hydrochloricus acid: this has already been referred to under chemical incompatibility.

Most of the synthetic remedies are insoluble in water. Phenacetin, acetanilide, acetylsalicylic acid,[1] etc., should preferably be prescribed in cachets. Phenazone (antipyrin) is an exception, being freely soluble. The synthetic hypnotics are practically insoluble in cold water. They are, however, much more soluble in hot liquids, and if given in this way are rapidly absorbed and eliminated, and the after-effects are less marked. Barbitone (veronal), being an acid, can be dissolved by means of an alkali: veronal-sodium has been introduced as a soluble form.

Iodine is practically insoluble in water, but is freely soluble in potassium iodide solution.

The organic silver compounds are as a rule soluble in water. Argyrol is soluble in all proportions; silver proteinate (protargol) is soluble (with careful dispensing) to the extent of 1 : 2.

Alcohol as a solvent is much more limited than water in its scope. Many of the water-soluble metallic salts are

[1] Acetylsalicylic acid (aspirin) is dissociated in contact with water. Its calcium, lithium, and magnesium salts, however, are readily soluble and are now frequently prescribed.

insoluble in alcohol, and the addition of any spirituous preparation, such as a tincture, often throws such salts out of solution. Sodium bicarbonate, for example, is soluble in 11 parts of water, and a mixture containing this salt in any quantity near saturation (say ʒiv in ℥vi) will not stand the addition of a tincture or a spirit.

Resins, as a rule, are soluble in alcohol, while gums are soluble in water. Alcoholic solutions of resins are precipitated by water, but the precipitate may be held in suspension by means of a gum. That is the reason why certain gum-resins, such as myrrh and ammoniacum, form emulsions with water.

Gums are insoluble in alcohol. Mucilage of acacia should not be prescribed with strong tinctures, though it is useful as a suspending agent when a resinous tincture is contained in an aqueous mixture. (See *Immiscibility*, p. 23.)

It is well to remember that the only fixed oils soluble in alcohol are castor and croton oils. Castor oil is freely soluble in rectified spirit (90 per cent. alcohol). Croton oil is soluble in absolute alcohol and in strong solution only; the solubility depends greatly on the age and condition of the oil.

Glycerin is a useful solvent. Itself miscible with water or alcohol in all proportions, it is a good solvent for tannic acid, iodine, carbolic acid, alum, corrosive sublimate, etc. Glycerin of carbolic acid (1 : 5) is readily miscible with water, and may be used for the preparation of strong aqueous solutions of phenol. Glycerin is a good preservative, forming the basis of a series of 'non-alcoholic' tinctures and extracts.

The use of the fixed oils is limited. Castor oil is a valuable solvent for alkaloids when these are to be instilled into the eye. Such solutions may be ordered of atropine, cocaine, homatropine, eserine, etc., from ½ to 2 per cent. The basic alkaloids must be used; not their salts, which are insoluble. Olive oil or liquid paraffin are good solvents of menthol for application as a spray.

Ether and chloroform are not much used as solvents in dispensing practice. The former dissolves alkaloids, fats, resins, iodine, etc., while the latter is frequently ordered in liniments to promote absorption and allay pain. Camphor or mastiche may be dissolved in chloroform as an application in toothache; menthol and chloroform are sometimes used with other ingredients as an inhalant. It may be mentioned here that chloroform itself is very slightly soluble in water (1 : 200) and freely soluble in spirit. Spirit of chloroform (1 : 20) should therefore be prescribed cautiously with aqueous mixtures, as unless there is also a fair proportion of spirit in the form of tinctures, etc., the chloroform is liable to be thrown out and to collect in globules at the bottom of the bottle.

Cocaine hydrochloride, dissolved in chloroform water, throws out globules of chloroform. This may be prevented by the addition of about 5 per cent. of alcohol.

(*b*) **Immiscibility.**—When drugs are to be exhibited in a vehicle in which they are insoluble, certain rules must be observed regarding their miscibility with that vehicle. Oils and resinous tinctures, for example, are not miscible with water, and yet with proper precautions these may be exhibited in an aqueous medium. Insoluble salts, such as those of bismuth, may be suspended in water by suitable means.

A mixture of an oil with water is known as an *emulsion.* The preparation of an emulsion is an art in itself, and the *modus operandi* should always be left to the pharmacist. In a perfect emulsion the globules of oil should be so minute and so perfectly coated with gum or other emulsifier as to remain permanently suspended. Milk, for example, is an ideal emulsion. The quality of an emulsion is as much a question of manipulation as of ingredients, and the best form of prescription for such simply indicates the dose and the total volume, instructing the dispenser to make an emulsion *secundum artem* :—

℞ Paraffini liquidi - - - - ℥ii.
Aquam - - - - ad ℥vi.

Fiat emulsio secundum artem cujus ℥ss ter in die capiat.

In the case of resinous tinctures and liquid extracts, which become milky on addition of water, a similar rule applies. It frequently happens that the tincture or extract itself, or some other ingredient in the mixture, contains an emulsifying agent. When this is not the case the resin will soon coalesce and cause complete separation of the active ingredient, and an emulsifier, such as mucilage of acacia, will be required. This difficulty may safely be left to the pharmacist, who always knows just when to add an emulsifier, and to what extent.

In short, whenever anything of the nature of an emulsion is required, the physician's rule is a simple one :—Write your prescription, add the words *secundum artem*, and leave the pharmacist to do the rest.

When insoluble salts, such as those of bismuth, have to be suspended in water, a suspending agent may or may not be necessary. Most bismuth salts are now prepared in light form for dispensing, and the customary instruction to 'shake the bottle' is all that is necessary. One point may be emphasized here. Pulv. tragacanth. co. ought not to be prescribed with bismuth subnitrate, as very inconvenient clotting results when the bismuth salt is at all acid.

The question of miscibility arises also in the case of certain outward applications. It is well to remember, when writing a

prescription, that lanolin is the only fatty substance miscible with water to any extent. Lard, simple ointment, and vaseline will absorb from 12 to 20 per cent. of their weight of water, but lanolin will take up more than its own weight. Oils are miscible with one another as a rule, but castor oil and liquid paraffin separate into layers, although at first they appear to be miscible. Glycerin is not miscible with oils. Alkalis and oils form a soapy emulsion when mixed; for example, liquid ammonia mixes with camphor liniment, to form the well-known 'camphorated oil and hartshorn.'

(*c*) **Undesirable Change of Colour.**—The principal difficulties under this head have already been discussed in the section dealing with chemical incompatibility. These are: the black colour formed by salts of iron with tannin; the red colour produced when ferric chloride is mixed with salicylates, acetates, or bromides; the trouble experienced when spirit of nitrous ether is brought into contact with certain substances; and some other cases. (See p. 18.)

Infusion of roses is prepared with sulphuric acid in order to bring out the beautiful red colour of the petals. This red colour changes to bright green in presence of alkalis, consequently an excess of alkali added to a mixture containing this infusion will colour the mixture green. Magnesium carbonate or potassium citrate or acetate will produce this change, as in the following mixture :—

℞	Heroin. hydrochlor. - - -	gr. i.
	Vin. ipecac. - - - -	℥ii.
	Potass. citrat. - - - -	℥iii.
	Glycerin. - - - - -	℥i.
	Infus. rosæ acid. - -	ad ℥vi.

(*d*) **Unsuitable Consistence or Excessive Bulk.**—These are pitfalls to be avoided in the prescription of pills and powders. Pills should never exceed five grains in weight, and this should include due allowance for any excipient that may be necessary. It is unwise to order five grains of, say, powdered rhubarb in a pill, because the necessary excipient will increase the bulk excessively. The exact excipient to be used should generally be left to the discretion of the pharmacist. Deliquescent substances, as a rule, are unsuitable for prescription either in powder or pill form.

(*e*) **Molecular Change.**—The most familiar example of molecular change is the formation of a liquid or semi-liquid from the combination of two solids. Camphor forms a liquid with such substances as chloral hydrate, menthol, and carbolic acid, and such combinations are frequently prescribed intentionally.

Phenazone (antipyrin) should not be prescribed in powder form with sodium salicylate or with acetanilide for the same reason. Phenacetin or acetanilide forms a pasty mass with salicylic acid, as does also hexamine with acetylsalicylic acid. Chloral hydrate and sulphonal also become pasty when mixed. When sodium sulphate is mixed with potassium citrate, water of crystallization is liberated and the powder becomes semi-liquid.

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3. Therapeutic Incompatibility

The question of therapeutic incompatibility hardly comes within the scope of these pages, but there are one or two points which might well be borne in mind. Medical men are not likely to prescribe drugs that are antagonistic in therapeutic action, but it happens occasionally that remedies are prescribed in a form that modifies or even neutralizes their effect on the organism. For example, W. G. Smith[1] records a case in which a patient's face was stippled with black dots of mercury sulphide as the result of a mercurial application followed by a preparation of sulphur. A similar result may follow the internal administration of mercurials simultaneously with the external application of sulphur, or *vice versa.*

The following ointment is said by Wyatt[2] to have caused unexpected results:—

℞ Unguent. iodi - - - - ℥iss.
Ung. hydrarg. fort. - - - ℥ss.

The ointment was applied to a glandular swelling in the neck, but proved so severe that its use had to be stopped. Iodide of mercury was formed, and this, in practically a nascent condition, penetrated the skin so deeply that severe blistering was caused. A similar result followed the external application of iodine in a case where mercurial ointment had been applied some days previously.

Sometimes external and internal treatment, when administered simultaneously, may prove therapeutically incompatible. A case has been cited in which hydrogen peroxide was applied externally, while potassium iodide was given internally. The nascent iodine caused severe burning in the skin.

Mercurial preparations, as has already been pointed out, should be avoided in the case of patients taking an iodide, such as potassium iodide, or syrup of iodide of iron. Severe irritation of the eye has been caused by the application of Pagenstecher's ointment in a patient under iodide treatment.

[1] *Incompatibility and Some of its Lessons*, by Walter G. Smith (1911).
[2] Harold Wyatt: *Evans' Journal*, 1912.

Crocker reports the case of a lad who, after taking ichthyol internally for an erythematous eruption of the face, used a 'lactate of lead lotion' (solution of subacetate of lead ℥i, fresh milk ℥ii). Soon the pores of his skin were blackened through the formation of lead sulphide.

The question of therapeutic incompatibility may arise in regard to the selection of an ointment base. A case occurred in the writer's experience of a gentleman who received a mercurial ointment prepared with lanolin for application in a kind of ringworm. Very soon symptoms of mercurial poisoning became manifest. The ointment was at once stopped, and replaced by another having a paraffin basis. The symptoms subsided, and did not reappear, although the second ointment was continued for some time.

When tincture of strophanthus is prescribed in aqueous mixture the glucoside gradually undergoes hydrolysis, and after some weeks the mixture is liable to produce disagreeable purgation, with little or no effect on the heart.[1]

It should be borne in mind that the digestive ferments, pepsin and pancreatin, are very liable to be 'put out of action' if ordered with other drugs. A very elaborate research on enzyme action, described in the *Extra Pharmacopœia*, shows how readily this action is interfered with. Among the more important drugs which inhibit the action of pepsin may be mentioned: alcohol, alkalis, malt extract, magnesium sulphate, paraldehyde, potassium salts (chloride, bromide, iodide), sodium chloride, hexamine.

[1] P. M'Ewan: *Art of Dispensing*, p. 380.

Part II

A Dictionary of Incompatibilities

PART II

A DICTIONARY OF INCOMPATIBILITIES

NOTE.—All drugs are arranged alphabetically under their English names. In the case of those official in the B.P., the official name is used, the more usual synonyms being added. In the General Index at the end of the book the figures in heavy type refer to items in Part II.

IN the following pages the examples of incompatibility already discussed are summarized under the names of the drugs. In addition such useful data as doses, solubility, etc., are added.

Acacia. Gum Arabic.

SOLUBILITY.—Almost completely soluble in water; insoluble in alcohol.

Mucilage of acacia (the solution in water) is slightly acid to litmus; the acidity varies with different samples, but will not cause trouble unless decomposition has begun. Decomposition may be prevented by addition of 0·1 per cent. benzoic acid (Ext. Ph.).

INCOMPATIBILITY.

Acids.—Sulphuric acid, or strong solution of a sulphate, will precipitate calcium sulphate, setting free arabic acid. Nitric acid decomposes the gum.

Alcohol.—Gum acacia is insoluble in alcohol. Addition of a strong spirit or tincture may therefore precipitate the gum from a mixture containing mucilage. If so, addition of water will redissolve the precipitate.

Alkaloids.—Acacia prevents the precipitation of alkaloids by tannic acid or by Mayer's reagent (potassium mercuric iodide). It gives coloration with morphine, eserine, and adrenalin.

Borax.—Borax in strong solution forms a thick unsightly precipitate with gum acacia. This may be prevented if borax solution and mucilage are both diluted with water. Glycerin added in small quantity to the borax solution decomposes the borax and prevents coagulation.

Guaiacum.—Acacia gives a blue colour with tincture of guaiacum. This colour may not appear if the guaiacum is old.

Iron.—Ferric salts coagulate mucilage of acacia, but ferrous salts do not. Dialysed iron forms a red gelatinous mass (Ruddiman).

Lead.—Lead subacetate forms with mucilage of acacia a thick unsightly precipitate. Lead acetate does not form such a precipitate.

Acetanilide. Antifebrin.

DOSE.—2 to 5 grains (0·12 to 0·3 gm.).

Acetanilide (*continued*).

Solubility.—Water 1 : 210 ; boiling water 1 : 18 ; glycerin 1 : 100 ; alcohol (90 p.c.) 1 : 4·2 ; brandy about 1 : 20. Chloral hydrate increases the solubility in water.

Lapthorn Smith suggests that the dose be put in a tumbler, a tablespoonful of alcohol or two tablespoonfuls of wine added (in which the acetanilide partially dissolves), the tumbler filled with hot water, and the mixture sweetened with sugar.—Prescriber, Sept. 1923, p. 307.

Incompatibility.

Acetanilide forms a more or less pasty mass with chloral hydrate, phenazone, phenol, or salicylic acid.

With spiritus aetheris nitrosi it forms a yellow solution.

With bromine it gives a white precipitate.

Acetanilide is hydrolysed by acids generally.

Acetates.

Solubility.—Nearly all acetates are soluble in water and in alcohol. Exceptions are quinine, silver, and mercurous acetates. Lead acetate when exposed to air loses some of its acetic acid and absorbs CO_2, forming insoluble carbonate.

Incompatibility.

Acids.—Stronger mineral acids combine with the base and liberate acetic acid. Sulphuric acid with alcohol (aromatic sulphuric acid) liberates acetic ether or ethyl acetate.

Iron.—All soluble acetates give a red colour with ferric salts.

Quinine.—Soluble acetates give with quinine salts a bulky precipitate of quinine acetate.

Spirit. Aetheris Nit.—Potassium acetate mixed with spirit. aetheris nit. causes effervescence, due possibly to liberation of ethyl nitrite (Ruddiman).

Acetic Acid (*see also* Acetates *and* Acids).

Solubility.—Mixes with alcohol and ether in all proportions. The strong acid dissolves resins, gelatin, fibrin, and albumin.

Incompatibility.

Acetic acid is contained in oxymel of squill and in syrup of squill ; these preparations therefore show the same incompatibilities.

Alcohol with sulphuric acid liberates acetic ether or ethyl acetate.

Carbonates.—In common with other acids, acetic acid liberates CO_2 from carbonates and bicarbonates.

Alkalis.—Forms acetates with alkalis.

Quinine.—Acetic acid increases the solubility of quinine sulphate in water.

Acetylsalicylic Acid. 'Aspirin.'

Dose.—5 to 15 grains (0·3 to 1·0 gm.) in cachets, tablets, or suspension.

Acetylsalicylic Acid (*continued*).

Solubility.—Water 1 : 300 ; alcohol 1 : 5. Addition of sodium citrate increases its solubility in water, but some decomposition probably occurs. The calcium, magnesium, and lithium salts are readily soluble in water.

Incompatibility.—Water (or moisture) decomposes it into acetic and salicylic acids. The incompatibles of these acids are therefore contraindicated.

The powder should not smell of acetic acid, nor should it give a violet colour with ferric chloride.

Hexamine forms a paste with the dry powder.

Alkalis decompose it forming acetates and salicylates. Carbonates liberate CO_2.

Potassium Iodide is decomposed, iodine being set free. In cachets this may combine with the starch forming an unsightly blue-black colour.

Quinine.—The statement that quinine forms a toxic compound with acetylsalicylic acid is not correct. Quinine and acetylsalicylic acid may be prescribed together in a *mixture*, the resulting quinine acetylsalicylate being soluble in water. *Powders* of quinine and aspirin are liable to decompose liberating salicylic acid in course of time.

Acids, Mineral.

Incompatibility.

Alkaline preparations, such as liquor arsenicalis, spirit. ammon. aromat., linim. camph. ammon., lime water, liquor bismuthi, ammoniated tinctures, alkali salts.

Acacia, Mucilage of.—*See* Acacia.

Adrenalin.—Nitric and nitrohydrochloric acids oxidize adrenalin ; other dilute mineral acids, if free from iron, are compatible.

Alkaline carbonates, which produce effervescence ; chalk mixture, grey powder, etc.

Hyposulphites.—Sulphur liberated.

Iodides.—Iodine liberated.

Liquorice, Extract of.—Glycyrrhizin precipitated.

Organic Salts.—Salicylates, benzoates, cinnamates, etc. Organic acid liberated.

Adrenalin, B.P. 1914.

Synonyms.—Epinephrine, U.S.P. (X.) ; Adrenine ; Renaglandin ; Hemisine ; Vaso-Constrictine.

Dose (Epinephrina, U.S.P.), 0·5 mg. ($\frac{1}{120}$ grain) hypodermically.

Solubility.—Very slightly in water ; more readily in hydrochloric acid forming chloride. Usually prescribed as :—

Liquor Adrenalini Hydrochloricus, B.P. 1914. Strength 1 : 1000 with chloroform, sodium chloride, and diluted hydrochloric acid. Dose 0·6 to 1·8 c.c. (10 to 30 minims).

Stability.—Very liable to oxidation, by the air or by some oxidizing

Adrenalin (*continued*).

agent, and when oxidized is more or less inert. The acid in the official solution retards oxidation. When the solution has become pink or brown it should be discarded. Benzoic acid is said to be the best preservative.

INCOMPATIBILITY.—Anything that will promote oxidation : iodine, chlorine, potassium permanganate, nitrites, persulphates, peroxides, etc. Formaldehyde is incompatible.

Ordinary dilute mineral acids are compatible, except nitric and nitrohydrochloric acids, which act as oxidizing agents.

Alkalis not only neutralize the acid in the solution, but themselves promote oxidation. Ferric chloride hastens oxidation very rapidly, colouring the solution green. Traces of iron in any substance—even in the water or in the glassware—will hasten oxidation and render the solution inert in a short time. The hydrochloric acid used in making the official solution must be free from iron.

The action of adrenalin is destroyed by such diluents as glyco-thymoline, Dobell's solution, etc. The only safe diluent is normal saline solution (PRESCRIBER, 1925, May, 198).

It is safest *to prescribe adrenalin solution alone*, without any admixture.

Alcohol. Ethyl Alcohol 90 per cent. Spiritus Rectificatus, B.P.—The B.P. recognizes five strengths of ethyl alcohol : 90, 70, 60, 45, and 20 per cent.

The U.S.P. (X.) recognizes Alcohol (Ethanol), 94·9 per cent., and Diluted Alcohol, made by mixing this with an equal quantity of water.

MEDICINAL USES.—Mainly as a solvent for resins, essential oils, castor oil, etc., and for preparation of spirits, tinctures, liquid extracts, etc.

INCOMPATIBILITY.

Chloral Hydrate with alcohol (tinctures, etc.) forms oily drops of chloral alcoholate.

Gums are not soluble in alcohol. Mucilage of acacia should not be prescribed with strong tinctures, except as a suspending agent.

Mineral Acids convert alcohol into esters and ether.

Oxidizing Agents.—Chromic acid, chromates, and potassium permanganate oxidize alcohol to aldehyde and acetic acid.

Resins are soluble in alcohol ; the alcoholic solution is precipitated by water, but the precipitate may be held in suspension by a gum. Resinous tinctures must be combined with mucilage of acacia when ingredients of a mixture.

Water precipitates many substances from alcoholic solution.

Water-soluble Salts are frequently thrown out of solution in a mixture by presence of a tincture.

Alkalis.

This term embraces all preparations containing a carbonate or hydroxide of potassium, sodium, or ammonium, and to a certain extent

Alkalis (*continued*).

also the carbonates and hydroxides of calcium, lithium, strontium, barium, and magnesium. All ammoniated preparations are included, also potassium and sodium carbonates and bicarbonates, lime water, liquor arsenicalis, and liquor bismuthi. Chalk mixture and grey powder are incompatible with acids.

INCOMPATIBILITY.

Acid Preparations, *see* Acids

Alkaloids.—Addition of an alkali to a solution of an alkaloidal salt precipitates the basic alkaloid.

Calcium Salts.—Alkaline hydroxides precipitate calcium hydroxide from solutions of soluble calcium salts.

Iron.—Alkaline carbonates, hydroxides, and phosphates precipitate the corresponding salt of iron from solutions of soluble iron salts.

Oils form a soap with alkalis : in some cases this is desirable, *e.g.*, to form an emulsion.

Pepsin Preparations.—These invariably contain acid, and are incompatible with alkalis.

See also Carbonates.

Alkaloids.

SOLUBILITY.—Alkaloids (basic) as a rule are insoluble in water, but their salts are generally soluble, especially in an acid solution. Basic alkaloids are rendered soluble by addition of an acid, which forms a salt. Addition of alkali to this solution will precipitate the basic alkaloid.

If an alkaloid is prescribed with an effervescent mixture, it should be added to the *acid* portion. If prescribed with arsenic, liq. arsenici hydrochlor. should be ordered.

Basic alkaloids are generally soluble in castor oil ; this is a useful solvent for atropine, cocaine, eserine, etc., for application to the eye (0·5 to 2 per cent.).

INCOMPATIBILITY.

Acacia.—Gives coloration with morphine, eserine, and adrenalin.

Alkalis.—Alkalis, alkaline carbonates, ammoniated preparations, liquor arsenicalis, lime water.

Halogens.—Iodine and iodides ; bromides, etc.

Mercury.—Mercuric chloride ; Donovan's solution and potassio-mercuric iodide (except caffeine and theobromine).

Picric Acid precipitates quinine.

Salicylates and *Benzoates* precipitate most alkaloids.

Tannin.—Tannin itself and all infusions, etc., containing tannin. Acacia sometimes prevents precipitation.

N.B.—The incompatibility of alkaloids should be carefully studied : most of them are potent drugs, and precipitation or insolubility may result in an overdose.

Alum. Alumen, B.P. ; Aluminium and Potassium Sulphate.

Dose.—5 to 10 grains (0·3 to 0·6 gm.).

Solubility.—Water, 1 : 10 ; boiling water, 3 : 1 ; glycerin, 1 : 3 ; alcohol, insoluble.

Incompatibility.

Alkalis and alkaline carbonates, also borax and lime water, precipitate aluminium hydroxide. Precipitation is in some measure retarded by citrates, tartrates, or glycerin. Dry alum rubbed with borax becomes moist (*see* Borax).

Lead Acetate.—Precipitate of lead sulphate.

Tartaric Acid.—Precipitate of ' cream of tartar.'

All the incompatibilities of soluble sulphates.

Ammoniated Preparations. Aromatic spirit of ammonia, various ammoniated tinctures, etc.

Incompatibility (*see also* Alkalis).

Acids.—All acid preparations : liq. arsenici hydrochlor., syrups of lemon and squill, wines, aceta.

Alkaloids.—Basic alkaloids are precipitated by ammonia from solutions of their salts.

Calcium Chloride.—Precipitate of calcium hydroxide.

Chloral Hydrate.—Chloroform is liberated.

Copper, Iron, and Zinc Salt.—Precipitate of insoluble hydroxide.

Iodine.—Forms nitrogen iodide, highly explosive.

Oils.—A ' soap ' is formed. This may be intended, as in ' camphor oil and hartshorn.'

Pepsin Preparations.—Pepsin acts only in an acid medium, and its preparations usually contain acid. Ammoniated preparations are therefore incompatible.

Roses, Infusion of.—Colour changed to green.

Note.—Ammoniated tincture of quinine forms a milky suspension when mixed with water ; with aerated water a soluble carbonate is formed and the solution is clear.

Antimony, Tartarated. Tartar Emetic.

Dose.—$\frac{1}{25}$ to $\frac{1}{8}$ grain (2·5 to 8 mg.) ; as emetic $\frac{1}{2}$ to 1 grain (0·03 to 0·06 gm.).

Solubility.—Water, 1 : 17, solution slightly acid ; almost insoluble in alcohol ; moderately soluble in weak alcoholic liquids. Best prescribed in aqueous solution or as Antimonial Wine (1 : 250), dose 10 to 30 minims (0·6 to 1·8 c.c.), or as emetic 2 to 4 fluid drachms (8 to 16 c.c.). May also be given in pill.

Incompatibility.

Alkalis.—Hydroxides and carbonates precipitate antimony oxide. Citrates and tartrates prevent this precipitation. Lime water precipitates tartrates of calcium and antimony.

Antimony, Tartarated (*continued*).

Lead Salts give a precipitate with tartar emetic.

Mineral Acids precipitate the corresponding salt of antimony.

Soaps give a precipitate with tartar emetic.

Tannic Acid precipitates antimony tannate. Most vegetable infusions contain tannin.

Antipyrin, *see* Phenazone.

Apomorphine Hydrochloride.

Dose.—Hypodermically $\frac{1}{20}$ to $\frac{1}{10}$ grain (3 to 6 mg.); by mouth, $\frac{1}{10}$ to $\frac{1}{4}$ grain (6 to 16 mg.).

Solubility.—Water, 1 : 60; alcohol, 1 : 50. Solutions decompose and turn green on boiling or on keeping; acidification with a trace of hydrochloric acid will prevent this.

Incompatibility.—All alkaloidal precipitants (*see* Alkaloids).

Ammonia.—Develops a purple colour.

Iron Salts.—Red precipitate, turning black.

Argyrol.—*See* Silver, Organic Compounds.

Arsenic, Preparations of.

Arsenious acid is soluble in water 1 : 100; a solution of this strength, being neutral, is compatible with both acids and alkalis.

Arsenious acid in solution is precipitated by *iron salts* (basic arsenite), by *iodides*, *magnesia*, *lime water*, and *tannin* (vegetable infusions).

Liquor arsenicalis is alkaline and incompatible with acids; liquor arsenici hydrochloricus is acid and incompatible with alkalis and carbonates.

Liquor arsenii et hydrargyri iodidi (Donovan's solution) precipitates all alkaloids except caffeine and theobromine.

Barbitone. Diethylbarbituric Acid; 'Veronal.'

Dose.—5 to 10 grains (0·3 to 0·6 gm.). Part I poison.

Solubility.—Cold water, very slight; boiling water, 1 : 12; alcohol, 1 : 9; freely soluble in alkaline solutions. (Veronal-sodium or 'medinal' is the sodium salt and is freely soluble in water.) Best administered as tablets or cachets, or dissolved in hot water.

Incompatibility.—Of little moment, as barbitone is seldom administered along with any other drug.

Benzoates.

Incompatibility.

Acids.—The mineral acids, being stronger acids than benzoic, combine with the base of the benzoate and set benzoic acid free, which is precipitated in the form of crystals.

Alkaloids.—Alkaline benzoates precipitate most alkaloids.

Caffeine Citrate.—This is readily dissociated in aqueous solution,

Benzoates (*continued*).

citric acid being set free, which may combine with base, precipitating benzoic acid in the same manner as would a mineral acid.

Iron.—Ferric salts give a pink precipitate of ferric benzoate.

Lead, *Mercury*, and *Silver Salts* give precipitates.

Benzoic Acid.

Dose.—5 to 15 grains (0·3 to 1·0 gm.).

Solubility.—Water, very slight (1 : 450); alcohol, 1 : 3; ether, 1 : 2·5; chloroform, 1 : 7. Soluble in alkaline solutions forming benzoates (*q.v.*). The alcoholic solution is precipitated by addition of water.

Incompatibility.—Same as benzoates.

Bicarbonates.—*See* **Carbonates.**

Bichromates.—*See* **Chromic Acid.**

Bismuth, Liquor. Liquor Bismuthi et Ammonii Citratis, B.P.

Dose.—½ to 1 fluid drachm (2 to 4 c.c.).

Incompatibility.

Acids.—Being an alkaline preparation, liquor bismuthi has all the incompatibilities of alkalis, *i.e.* it is precipitated by acids, and precipitates alkaloids and iron salts.

Alkaloids.—Liquor bismuthi and potassium iodide form a double iodide which precipitates most alkaloids.

Bismuth Salicylate. (Bismuth Subsalicylate U.S.P.)

Dose.—5 to 20 grains (0·3 to 1·2 gm.).

Solubility.—Insoluble in water or alcohol. Usually prescribed in cachets, or as a mixture suspended with mucilage of acacia. If a 'light' salt is used, a suspending agent may not be necessary.

Incompatibility.

Carbonates.—Dissociation of the salt with effervescence. Instead of prescribing bismuth salicylate with sodium bicarbonate, it is better to order bismuth carbonate and sodium salicylate.

Iron Salts.—Gives a violet colour with ferric salts.

Bismuth Subnitrate. Bismuth Oxynitrate.

Dose.—5 to 20 grains (0·3 to 1·2 gm.).

Solubility.—Insoluble in water or alcohol. Soluble in hydrochloric or nitric acid. Slowly decomposed by water, forming basic nitrate and free nitric acid, therefore best prescribed in powder form. If suspended in water, a 'light' salt should be used; tragacanth or acacia should never be employed as suspending agent, as it causes inconvenient clotting when the salt is at all acid. The best suspending agent is glycerin, syrup, or compound infusion of gentian (Stannard: *Ph.J.* Jan. 9, '26, p. 33).

Bismuth Subnitrate (*continued*).

INCOMPATIBILITY.

Carbonates.—Sodium bicarbonate in a mixture with bismuth subnitrate will cause slow effervescence, which may burst the bottle. Bismuth carbonate should be prescribed with sodium bicarbonate. For the same reason bismuth subnitrate should not be prescribed with chalk mixture, which contains calcium carbonate.

Glycerin.—Possible formation of nitroglycerin, and danger of explosion.

Iodides.—Bismuth iodide formed.

Sulphur.—Bismuth sulphide formed.

Tannic Acid.—Yellow bismuth tannate formed slowly in presence of water.

Borax. Sodium Biborate.

DOSE.—5 to 15 grains (0·3 to 1·0 gm.).

SOLUBILITY.—Water, 1 : 25 ; alcohol, insoluble ; glycerin, 1 : 1. Borax is decomposed by glycerin forming boric acid and glyceryl borate ; glycerin of borax is therefore acid and incompatible with carbonates. Borax helps the suspension of oils and resins.

INCOMPATIBILITY.

Acacia.—Borax coagulates mucilage of acacia (*see* Acacia).

Acids.—Aqueous solution of borax is alkaline, and mineral acids precipitate boric acid. With most metallic salts of mineral acids borax forms an insoluble double salt.

Alkaloids.—Borax, being alkaline, precipitates cocaine and most alkaloids. Prior addition of glycerin to the borax makes an acid solution (see above) and prevents precipitation.

Alum.—Alum powder triturated with borax powder forms a moist combination, due to liberation of water of crystallization. Solution of borax with alum precipitates aluminium borate.

Zinc.—Zinc sulphate and borax in solution throw out zinc borate.

Caffeine. Theine.

DOSE.—1 to 5 grains (0·6 to 0·3 gm.).

SOLUBILITY.—Water, 1 : 80 ; alcohol, 1 : 40. Solubility in water increased by addition of phenazone, sodium salicylate, or sodium benzoate ; also by acids, but as it is a feeble base acid solutions are apt to split up, caffeine separating.

INCOMPATIBILITY.—Caffeine is *not* precipitated by the usual alkaloidal reagents (*see* Alkaloids), but from strong solutions it is precipitated by tannic acid, silver nitrate, and mercuric chloride

Caffeine Citrate.

DOSE.—2 to 10 grains (0·12 to 0·6 gm.).

SOLUBILITY. — Water, 1 : 32 ; alcohol, 1 : 25. It is soluble in 4 parts of hot water, but further addition of water throws out the

Caffeine Citrate (*continued*).

caffeine, which is redissolved in 32 parts of water. There is no advantage in prescribing caffeine citrate in solution : it is much weaker than pure caffeine (50 per cent.) and is relatively no more soluble ; it is incompatible with certain drugs (see below) and is readily dissociated in solution. Best prescribed in cachets, or as Effervescent Caffeine Citrate.

Incompatibility.—Solution of caffeine citrate contains citric acid, which will act on benzoates, salicylates, etc., as would a mineral acid, setting free the organic acid. For such combinations pure caffeine should be used. In combination with potassium iodide and spirit of nitrous ether iodine is set free.

Calcium Salts.

Solubility.—The chloride and bromide are the only salts freely soluble in water. Calcium lactate is fairly soluble when fresh (about 1 : 20), but becomes less soluble on keeping. A good prescription for calcium lactate is to dissolve calcium carbonate in lactic acid and water. The hypophosphite, acetylsalicylate, and glycerophosphate are moderately soluble. The hydroxide is soluble about 1 : 900, lime water being a saturated solution ; solution is greatly assisted by addition of sugar, as in saccharated solution of lime.

Incompatibility (*see also* Alkalis).—The principal insoluble salts of calcium are the hydroxide, carbonate, sulphate, phosphate, tartrate, and oxalate. Solutions of the soluble salts should not, therefore, be combined with anything likely to precipitate these salts. For example : calcium chloride and aromatic spirit of ammonia ; calcium bromide and sodium sulphate ; lime water and tartar emetic.

Acids.—Calcium carbonate (chalk) effervesces with acids ; it is contained in chalk mixture and in grey powder. Grey powder is incompatible with confection of sulphur, which contains an acid tartrate.

For remarks on calcium hypophosphite, *see* Hypophosphites.

Note.—Lime water combines with oils to form a soapy emulsion, as in linimentum calcis and ' carron oil.'

Calomel.—*See* Mercury Subchloride.

Camphor.

Dose.—2 to 5 grains (0·12 to 0·3 gm.).

Solubility.—Water, 1 : 700 ; alcohol, 1 : 1·25 ; chloroform, 4 : 1 ; olive oil, 1 : 4. Water added to alcoholic solution (spirit of camphor) throws out the camphor. A strong solution of a metallic salt, such as potassium bromide, will throw out camphor from camphor water.

Incompatibility.—Camphor forms a liquid with chloral hydrate, menthol, phenol, thymol, naphthol, salol, salicylic acid, and some other substances. Such liquid combinations are often prescribed intentionally, as chloral-camphor, menthol-camphor, phenol-camphor, etc.

Carbolic Acid. Phenol.

Dose.—1 to 3 grains (0·06 to 0·2 gm.).

Solubility.—Freely soluble in alcohol, ether, chloroform, glycerin, fixed and volatile oils, solutions of alkalis. The crystals are permanently liquefied by addition of 10 per cent. of water, and the liquid carbolic acid so prepared is soluble in 12 parts of water. Carbolic lotion is usually of a maximum strength of 1 in 20; should it be required stronger it is better to dilute the glycerin of carbolic acid (1 : 5) to the required strength. Solution of phenol in liquid paraffin is liable to separate if stronger than 1 per cent. (Martindale).

Carbolic acid becomes pink on exposure to air.

Incompatibility.

Albumin is coagulated by carbolic acid.

Ammonia forms a colourless solution, turning to green and later to blue.

Carbonates do *not* effervesce with carbolic acid.

Collodion is gelatinized.

Copper, *Mercury*, and *Silver Salts* are reduced.

Hydrogen Peroxide oxidizes carbolic acid.

Iron.—A dilute solution of ferric chloride gives a violet colour.

Lead.—Solution of lead subacetate (not lead acetate) gives a white precipitate, which is said to be preventable by addition of glycerin, or a trace of acetic acid.

Liquid Combinations.—Carbolic acid forms liquid combinations with camphor, acetanilide, phenazone, chloral hydrate, menthol, and some other substances.

Nitric Acid forms trinitrophenol or picric acid.

Oil of Theobroma is softened by mixture with phenol, hence the addition of white beeswax in the official suppositories.

Potassium Permanganate oxidizes phenol to oxalic acid and carbon dioxide.

Spirit of Nitrous Ether gives a yellow colour changing to brown.

Carbonates and Bicarbonates.

Solubility.—The carbonates and bicarbonates of potassium, sodium, and ammonium are soluble in water; other carbonates are insoluble, but in some cases may be rendered soluble by addition of excess of carbon dioxide. All carbonates are insoluble in alcohol.

Incompatibility.

Acids.—Carbonates and bicarbonates effervesce in contact with acids (except hydrocyanic and carbolic acids) and with some acid salts.

Alkaloids.—Carbonates precipitate alkaloids from solutions of their salts.

Bismuth Subnitrate causes effervescence with an alkaline carbonate; bismuth carbonate does not.

Carbonates and Bicarbonates (*continued*).

Metallic Salts.—Carbonates of potassium and sodium precipitate most of the common metals : magnesium, calcium, barium, iron, silver, mercury, antimony, copper, zinc, etc. Ammonium carbonate does the same, but not with mercury, copper, or silver.

Castor Oil.

Solubility.—Castor oil is one of the two fixed oils soluble in rectified spirit (croton oil is the other).

Castor oil is apparently miscible with liquid paraffin, but the mixture soon separates into layers.

Castor oil is a useful solvent for alkaloids when these are to be instilled into the eye. Atropine, cocaine, novocaine, homatropine, eserine, etc., may be so used, strength 0·5 to 2 per cent. The basic alkaloids must be used ; not their salts, which are insoluble in oil.

Chloral Hydrate.

Dose.—5 to 20 grains (0·3 to 1·2 gm.).

Solubility.—Very freely soluble in water (4 : 1), in alcohol, and in ether ; also in chloroform 1 : 3, and in oils and fats. Chloral hydrate in concentrated aqueous solution is a good solvent for resinous matter (Ruddiman).

Incompatibility.

Alkalis.—Alkaline carbonates or hydroxides set free chloroform and produce a formate of the base.

Bromides and Iodides, in presence of alcohol, produce an oily layer of chloral alcoholate. It is unwise to prescribe chloral hydrate and potassium bromide with a tincture.

Camphor.—Chloral and camphor form a liquid combination. Sulphonal, trional, and several other solids also form liquids with chloral.

Potassium Permanganate oxidizes chloral hydrate.

Chloramine-T.

Dose.—½ to 3 grains (0·3 to 0·2 gm.), mixed with charcoal. Has been known to decompose in the stomach with liberation of chlorine gas (Prescriber, 1920, June, 257).

Solubility.—Water, 1 : 7 ; glycerin, 1 : 7 ; alcohol, 1 : 12 (see incompatibilities, below). Insoluble in liquid paraffin. As an antiseptic a 2 to 4 per cent. solution is used.

Incompatibility.—Chloramine-T is decomposed in presence of many substances, and should not be mixed with any other antiseptic.

It attacks metals, and should not be used to sterilize instruments.

The following drugs are definitely incompatible with chloramine-T : Acids and acid salts ; alcohol ; ammonia ; ammonium chloride ; boric acid ; gluside (saccharin) ; glycerin ; hydrogen peroxide ; soap ; sodium citrate ; sugar.

Chloramine-T (*continued*).

The following are compatible : Borax ; saccharin, soluble ; sodium chloride, carbonate, and bicarbonate ; starch ; talc ; zinc stearate (Kopfstein : *Amer. J. Pharm.*, Feb. 1923, p. 101).

Chlorates.

Solubility.—Metallic chlorates are soluble in water. Potassium chlorate is soluble 1 : 16 of water : solutions should therefore contain not more than 30 grains in an ounce.

Incompatibility.—Potassium chlorate (the salt generally employed) is a dangerously explosive drug, and should not be mixed with any reducing agent, such as arsenic, cyanides, phosphorus or hypophosphites, sulphur or hyposulphites, nitrites, oxalates, pyrogallol, ferrous or mercurous salts, reduced iron, formaldehyde, or organic substances such as sugar, tannin (vegetable drugs), glycerin, etc. Compound liquorice powder contains sulphur. It is best to avoid combination of any kind and to prescribe chlorates alone or in aqueous solution.

Addition of hydrochloric acid to a chlorate liberates chlorine gas : this reaction is taken advantage of in preparation of chlorine gargle.

Chloroform.

Dose.—1 to 5 minims (0·06 to 0·3 c.c.).

Solubility.—Water, 1 : 200 ; alcohol, freely.

Incompatibility.—Spirit of chloroform (1 : 20) in aqueous mixtures may throw out globules of chloroform, unless there is a fair proportion of spirit in the form of tinctures, etc., to retain it in solution.

Cocaine hydrochloride, dissolved in chloroform water, throws out globules of chloroform. This may be prevented by the addition of 5 per cent. of alcohol.

Chloroform is liable to decomposition and should be preserved from light, air, and heat.

Chromic Acid. Chromic Anhydride.

Solubility.—Freely in water. Chromates of the alkalis are soluble in water ; other chromates sparingly soluble. Chromic acid, being very deliquescent, should be kept in well-stoppered bottles, and should be protected from light.

Incompatibility.—Chromic acid is a powerful oxidizing agent, and contact with alcohol, glycerin, volatile oils, and other organic substances causes decomposition with explosive violence. Bichromates, in presence of mineral acids, tannin, sugar, etc., behave similarly. Potassium bichromate precipitates many of the alkaloids from solutions of their salts.

Cinchona.

Cinchona bark contains sufficient tannin to yield a precipitate with certain metallic salts, and to give a blue-black colour with iron salts.

Cinchona (*continued*).

As it contains alkaloids (quinine, etc.) it is incompatible with alkaloidal precipitants (*see* Alkaloids).

Cocaine and Salts.

Solubility.—The salts of cocaine generally are soluble in water. The basic alkaloid is insoluble in water but is soluble in oils. A solution in castor oil is used for eye drops. The alkaloid may be used in making ointments.

Incompatibility (Salts).

Alkaloidal Precipitants.—See Alkaloids.

Borax.—Precipitates the hydrochloride as hydrate. This may be prevented by the use of equal parts of borax and boric acid.

Chloroform Water.—See Chloroform.

Mercurochrome is precipitated by salts of cocaine.

Mercury.—An eye ointment containing yellow mercuric oxide and cocaine hydrochloride may cause severe irritation, due probably to formation of mercuric chloride. Cocaine hydrochloride with calomel, in presence of moisture, forms a grey or black mixture, due to reduction of mercury.

Phenol.—Cocaine hydrochloride is incompatible with phenol in presence of water, but is compatible in presence of alcohol or glycerin.

Silver.—Cocaine hydrochloride with silver nitrate precipitates silver chloride : cocaine nitrate should be used.

Copper Sulphate.

Dose.—(Astringent) $\frac{1}{4}$ to 2 grains (0·016 to 0·12 gm.). (Emetic) 5 to 10 grains (0·3 to 0·6 gm.).

Solubility.—Water, 1 : 3·5 ; very soluble in glycerin ; insoluble in alcohol.

Incompatibility.

Alkalis.—Alkali hydroxides (ammonia, lime water, etc.) precipitate copper hydroxide ; this is prevented by citrates, tartrates, and salicylates. Ammonia solution and ammonium carbonate form a precipitate which redissolves in excess forming a deep-blue solution. Alkaline carbonates precipitate copper carbonate, and alkaline phosphates precipitate copper phosphate. Borax also forms an insoluble compound.

Iodides.—Soluble iodides precipitate cuprous iodide and liberate iodine.

Tannin.—Tannin and vegetable astringents precipitate copper salts.

Creosote.

Dose.—1 to 5 minims (0·06 to 0·3 c.c.).

Solubility.—Water, about 1 : 150 ; freely in alcohol, ether, chloroform, glycerin, or glacial acetic acid.

Creosote (*continued*).

INCOMPATIBILITY.

Collodion.—In excess, forms a jelly.

Iron.—Gives a blue colour with ferric salts.

Lead.—Gives a white precipitate with lead subacetate.

Metallic Salts.—Reduces many metallic salts to the metallic condition.

Silver.—Triturated with silver oxide reacts with explosive violence. The same happens with strong oxidizing agents.

Diamorphine Hydrochloride.

Diacetylmorphine ('Heroin') Hydrochloride.

DOSE.—$\frac{1}{25}$ to $\frac{1}{8}$ grain. ('Dangerous drug.')

SOLUBILITY.— Water, 1 : 3 ; alcohol (90 p.c.), 1 : 11.

INCOMPATIBILITY.—Same as morphine. Alkaloidal reagents generally. Easily decomposed by acids and alkalis, forming morphine.

Digitalis.

INCOMPATIBILITY.—Preparations of digitalis (infusion, tincture, etc.) are incompatible with iron (the blackening may be prevented by citric acid—Martindale) ; with preparations of cinchona, and with lead acetate.

Ether.

SOLUBILITY.—Water, 1 : 10. Miscible with alcohol in all proportions. Dissolves alkaloids, fats, resins, iodine, etc., but is not much employed for this purpose in dispensing practice.

VARIETIES.—*Aether Purificatus, B.P.*, made from pure alcohol, for use as a general anaesthetic. *Rectified Ether* (S.G. 0·720) from methylated alcohol, is also used as a general anaesthetic when it stands the tests for purified ether. *Methylated Ether* (S.G. 0·717 to 0·719) is not adapted for production of general anaesthesia.

STABILITY.—Must be stored in amber glass bottles, well stoppered, and in a cool place. After exposure to light and air, ether acquires a strong oxidizing action, due to the formation of peroxides ; these are the cause of undesirable after-effects when the ether is used as an anaesthetic (Evers). The most important condition of storage is the exclusion of light ; the amount of air in the bottle has little effect. If carefully prepared and stored in amber glass bottles, little oxidation occurs, but the addition of 0·01 per cent. of pyrogallol has a powerful deterrent effect on the decomposition (Middleton).

Formaldehyde Solution.

An aqueous solution of formic aldehyde, 36 to 38 per cent. Used externally as an antiseptic, diluted with water in various proportions—1 : 50 up to 1 : 3000—according to its application.

Formaldehyde Solution (*continued*).

INCOMPATIBILITY.

Ammonia combines to form hexamine, and is therefore an antidote to formaldehyde poisoning.

Hydrogen Peroxide oxidizes it to formic acid.

Potassium Permanganate combines with evolution of heat, which drives off formic aldehyde vapour. This process is used for disinfection of rooms.

Formaldehyde is a strong reducing agent and is incompatible with adrenalin and other substances readily reduced.

On standing, solution of formaldehyde slowly deposits the crystalline paraformaldehyde.

Gallic Acid.

DOSE.—5 to 15 grains (0·32 to 1·0 gm.).

SOLUBILITY.—Cold water, 1 : 100 (one part with one part potassium citrate will dissolve in 30 of water); boiling water, 1 : 3; alcohol (90 p.c.), 1 : 8; ether, 1 : 50; glycerin, 1 : 3, with heat (Squire).

INCOMPATIBILITY.

Alkalis.—Effervescence and various colours.

Ammoniated Preparations.—Yellow or red colour with precipitate.

Iron Salts.—Blue-black colour or precipitate.

Potassium Permanganate.—Explosive reaction.

Spiritus Aetheris Nitrosi.—Red colour with effervescence.

An aqueous solution of gallic acid decomposes when exposed to air, giving off CO_2, and depositing a black substance (Ruddiman).

Gelatin.

Solutions of gelatin are coagulated by certain substances, such as tannic acid, picric acid, formaldehyde, etc.

After being heated for some time an aqueous solution of gelatin becomes incapable of gelatinizing.

Glucosides. Digitalin, Salicin, Strophanthin, etc.

Glucosides are decomposed (hydrolysed) in presence of mineral acids, alkalis, or enzymes. These enzymes are frequently present in the crude drug, and unless removed or destroyed are apt to cause decomposition of the tincture or other preparation.

Glucosides are generally precipitated by tannic acid or lead subacetate.

Glycerin.

DOSE.—1 to 2 drachms (4 to 8 c.c.).

SOLUBILITY.—Miscible in all proportions with water or alcohol; insoluble in chloroform, ether, or oils. Glycerin is a useful solvent for tannic acid, iodine, carbolic acid, alum, mercuric chloride, etc. As a sweetening agent it may be used to replace syrup, especially in cases where sugar is contraindicated.

Glycerin (*continued*).

INCOMPATIBILITY.

Borax.—Heated with borax a complex reaction occurs, the resulting 'glycerin of borax' being a new compound; in reality glycerin is not incompatible with borax. Some similar reaction takes place in the preparation of glycerin of boric acid.

Chromic Acid acts as other oxidizing agents (see below).

Nitric Acid forms the explosive nitroglycerin.

Oxidizing Agents may give an explosive reaction.

Potassium permanganate decomposes glycerin.

Glycerin prevents the precipitation in some cases of the heavier metals by alkali hydroxides.

Hexamine. Hexamethylenetetramine.

SYNONYMS.— Methenamine (U.S.P.); 'Urotropin.'

DOSE.—5 to 15 grains (0·3 to 1·0 gm.).

SOLUBILITY.—Water, 1 : 1·5; alcohol, 1 : 12·5; chloroform, 1 : 10; ether, insoluble.

INCOMPATIBILITY.—Requires care in administration with other drugs. When prescribed with acid sodium phosphate, the two drugs should be given separately and not in the same mixture, as formaldehyde is given off from a mixed solution. Powdered hexamine forms a liquid with acetylsalicylic acid; sodium benzoate or salicylate, salol, phenazone, etc., also cause decomposition. Hexamine is said to be incompatible with numerous other drugs, and to be decomposed by hot water, but we have been unable to confirm such statements. It is safest, however, to prescribe hexamine *per se*, to be taken with a large amount of water to prevent gastric irritation, and to give separately any other drugs required at the same time.

Hydrochloric Acid.

DOSE.—Diluted acid, 5 to 20 minims (0·3 to 1·2 c.c.).

INCOMPATIBILITY.—Same as mineral acids (*q.v.*). Forms insoluble chloride with salts of lead, mercury, and silver (most other chlorides are soluble). With potassium chlorate it liberates chlorine (*see* Chlorates).

Hydrocyanic Acid, Diluted.

DOSE.—2 to 5 minims (0·12 to 0·3 c.c.).

STABILITY.—Decomposes slowly on standing, and should be kept in a dark place, in small inverted stoppered bottles of amber glass. A small percentage of hydrochloric acid is said to retard decomposition.

INCOMPATIBILITY.

Alkalis.—Hydrocyanic acid is not therapeutically incompatible with alkalis such as sodium bicarbonate. The alkaline cyanide formed has practically the same therapeutic effect as the acid.

Hydrocyanic Acid, Diluted (*continued*).

Iron, Lead, and Silver Salts.—With soluble salts of these metals hydrocyanic acid forms insoluble cyanides.

Morphine.—Is said to form insoluble morphine cyanide, but our experiments do not confirm this.

Hydrogen Peroxide.

Liquor Hydrogenii Peroxidi, B.P., contains 10 volumes of available oxygen ; solutions containing 20, 30, and 100 volumes are also obtainable commercially.

Dose.—B.P. solution, $\frac{1}{2}$ to 2 drachms (2 to 8 c.c.).

Stability.—Has a tendency to decompose into water and oxygen ; stability may be ensured by presence of a slight excess of acid, or by addition of a small quantity of acetanilide.

Strong solutions produce transient irritation of the skin, lasting about an hour and with no after-effects.

Incompatibility.—On account of its powerful oxidizing properties, hydrogen peroxide should *never be prescribed in combination.* It is very liable to cause an explosive reaction. Care should be taken also in prescribing it along with other treatment : a case is reported in which it was applied externally while potassium iodide was given internally, with the result that the nascent iodine caused severe burning of the skin.

Hyoscyamine.

Dose.— $\frac{1}{200}$ to $\frac{1}{100}$ grain, increased.

Solubility. — Alkaloid : water, 1 : 120. Hydrobromide and sulphate : water, 2 : 1.

Incompatibility.—Same as alkaloids, but hyoscyamine is not precipitated by alkaline bicarbonates. The prescription of tincture of hyoscyamus with potassium bicarbonate is therefore quite in order.

Hypophosphites.

Solubility.—The hypophosphites of the metals are all soluble in water, except ferric hypophosphite, which is only slightly soluble.

Incompatibility —Hypophosphites readily form explosive compounds with oxidizing agents—chlorates, bromine and iodine, nitrates, permanganates, peroxides, etc. Hypophosphites have been known to explode when simply heated or triturated in a mortar.

Hyposulphites.—*See* Sodium.

Ichthyol. Ammonium Sulphoichthyolate.

Synonyms.—Ichthamol ; Ichthosulphol.

Dose.—15 to 30 grains (1 to 2 gm.).

Solubility.—Soluble in water, glycerin, oils, and in a mixture of alcohol and ether.

Incompatibility.

Acids.—Precipitate sulphoichthyolic acid as a sticky mass.

Alkalis.—Liberate ammonia.

Ichthyol (*continued*).

Alkaloids.—Double decomposition.

Alum.—Precipitate.

Potassium Iodide or *Bromide.*—Precipitate.

Zinc Sulphate.—Precipitate.

A case is reported in which the internal use of ichthyol with external application of lead lotion caused the pores of the skin to be blackened with lead sulphide.

Infusions.

Incompatibility.—Most vegetable infusions contain tannin, and are therefore incompatible with *alkaloids* and with *iron salts.* Infusions of quassia, calumba, and chiretta contain no tannin. *See also* Roses.

Iodine.

Solubility.—Iodine is practically insoluble in water, but is freely soluble in potassium iodide solution. Tincture of iodine, B.P. or U.S.P., contains potassium iodide and is miscible with water; the old 'Edinburgh' tincture and that of the French Codex, 1908, contain no iodide and are not miscible with water. In prescribing these last it is well to specify not only the source of the formula, but to add 'sine pot. iodid.'

Incompatibility.

Alkalis.—Decolorize iodine forming alkaline iodides.

Alkaloids.—Precipitate the insoluble hydriodide.

Ammonia.—Possibility of formation of nitrogen iodide (highly explosive). This applies to all ammoniated preparations, *e.g.*, linim. camph. co.

Essential Oils.—Some of these form explosive compounds with iodine, *e.g.*, turpentine.

Mercurial Ointments.—Formation of mercuric iodide is apt to cause severe irritation, even when the mercury and iodine are applied within a few days of one another.

Mercury Subchloride.—Precipitation of mercuric iodide. (A lotion containing calomel and tincture of iodine has been used with success in treatment of ringworm.)

Iodoform.

Dose.—$\frac{1}{2}$ to 3 grains (0·03 to 0·2 gm.).

Solubility.— Water, almost insoluble; alcohol, 1 : 100; ether, 1 : 8; chloroform, 1 : 12; oil of eucalyptus, 1 : 14; collodion, 1 : 10; olive oil, 1 : 30.

Incompatibility.—Exposed to sunlight, iodoform is decomposed. A mixture of *calomel* and iodoform changes colour (mercuric iodide) if exposed to sunlight, not otherwise. *Silver nitrate* decomposes iodoform, a violent reaction taking place if the drugs are mixed in the dry state. *Hydrogen peroxide* liberates iodine when the iodoform is in solution; dry iodoform does not seem to be affected by it.

Iron: Ferric Salts. Preparations of Ferric Chloride, Ferric Sulphate, etc.

INCOMPATIBILITY.

Acacia, Gum.—Thick precipitate.

Acetanilide.—Red colour in alcoholic solution only.

Acetates.—Blood-red colour : therapeutically admissible and harmless, as in Basham's mixture.

Adrenalin.—Traces of iron hasten oxidation of adrenalin and render its solution inert.

Alkaline Hydroxides (including Ammonia).—Precipitate of ferric hydroxide : previous dilution of the iron solution and addition of syrup or mucilage will render the mixture elegant. Citrates or tartrates will help to prevent precipitation.

Arsenates and *Arsenites.*—Precipitate.

Benzoates.—Flesh-coloured precipitate.

Carbolic Acid.—Violet coloration.

Gallic Acid.—Blue-black coloration.

Hypophosphites.—Precipitate.

Oils, Essential.—Some of these give a blue, green, or brown colour.

Opium.—Tincture of opium and ferric chloride give a red colour (ferric meconate).

Phenacetin and *Phenazone.*—Deep red colour.

Phosphates.—Precipitate of ferric phosphate, preventable by alkaline citrates or tartrates.

Potassium Iodide.—Tincture of ferric chloride liberates iodine ; scale preparations do not.

Salicylates (including Salol).—Deep purple colour of ferric salicylate ; properly dispensed this is not objectionable.

Tannin.—Iron tannate ('ink') : this applies to all vegetable drugs containing tannin.

Iron: Ferrous Salts. Ferrous Sulphate ; Syrup of Ferrous Iodide ; Saccharated Iron Carbonate ; Saccharated Iron Phosphate, etc.

INCOMPATIBILITY.

Alkalis.—Carbonates, hydroxides, and phosphates precipitate the corresponding salt of iron.

Potassium Chlorate with syrup of ferrous iodide liberates iodine.

Tannic and *Gallic Acids.*—Blue-black precipitate.

Ferrous salts are quickly converted to ferric salts on exposure to the air.

Lead Salts.

SOLUBILITY.—The acetate and nitrate are freely soluble in water ; most of the other salts are insoluble in water.

INCOMPATIBILITY.

Metallic Salts.—Lead acetate is incompatible with all soluble metallic

Lead Salts (*continued*).

salts the acid radical of which will form an insoluble lead salt : these comprise soluble oxides, carbonates, sulphates, chlorides, bromides, sulphides, iodides, phosphates, tartrates, benzoates, citrates, borates, salicylates, tannates, etc.

Acacia.—Gum arabic is precipitated by lead subacetate, but not by the acetate.

Alkaloids.—Precipitate with many alkaloids.

Carbolic Acid.—Gives a white precipitate with lead subacetate, but not with lead acetate.

Opium.—Precipitate of lead meconate.

Sulphur.—Forms lead sulphide. (Ichthyol contains sulphur.)

Tannin.—Any organic substance containing tannin will give a precipitate with lead acetate.

Dry lead acetate forms a soft mass when rubbed with alum, phenol, zinc sulphate, acetanilide, or salicylic acid.

Liquorice. Glycyrrhizae Radix, B.P.

Incompatibility.

Liquid Extract of Liquorice is incompatible with acids, glycyrrhizin being precipitated. This is soluble in alkalis, such as ammonia, but magnesium sulphate upsets this equilibrium, and a mixture containing liquorice, epsom salts, and ammonia is unsightly.

Compound Liquorice Powder contains sugar and sulphur and has the incompatibility of these substances. With potassium chlorate it forms an explosive mixture.

Lithium Salts.

Solubility.—The ordinary salts of lithium, with the exception of the carbonate and the phosphate, are soluble in water.

Incompatibility.—The soluble salts are therefore incompatible with soluble carbonates or phosphates. The benzoate and salicylate have also the incompatibility of benzoates and salicylates (*q.v.*).

Magnesium Salts.

Incompatibility.—Salts of magnesium behave very similarly to those of calcium—that is, they are precipitated by the alkaline hydroxides, carbonates, and phosphates—but they are compatible with bicarbonates and ammonium carbonate. Magnesium sulphate is compatible with sodium bicarbonate but not with sodium phosphate.

Heavy magnesia with magnesium sulphate in a mixture forms a hard insoluble mass. This does not occur if magnesium carbonate is used (*Chem. & Drug.*, 1928, 108, 521).

Menthol.

Dose.—½ to 2 grains (0·03 to 0·12 gm.).

Solubility.—Very slightly soluble in water ; insoluble in glycerin ;

Menthol (*continued*).
freely soluble in alcohol, ether, chloroform, olive oil, and liquid paraffin. Addition of water to an alcoholic solution throws out the menthol.

INCOMPATIBILITY.—Menthol forms a liquid mass with many substances, such as camphor, chloral hydrate, thymol, phenol, and resorcin. Such combinations are frequently prescribed intentionally for external application. Water added to an alcoholic solution of menthol throws out the menthol in the form of oily drops.

Mercurochrome. Mercurochrome-220 Soluble; Disodium-dibromo-hydroxymercury-fluorescein; Mercurome.

DOSE.—Intravenously, 2 to 5 mg. per kilo body-weight (2 to 5 grains for 10 stone) in 0·5 per cent. solution. By mouth, 1½ to 3 grains (0·1 to 0·2 gm.). As antiseptic for bladder irrigation, 1 per cent. solution; for other purposes up to 2·5 per cent.

SOLUBILITY.—Water, freely; alcohol, ether, chloroform, insoluble. (Alcohol dissolves a mere trace; this colours the liquid, but the solution is too weak to be of use.)

INCOMPATIBILITY.

Acids.—Precipitate the insoluble mercury compound.

Alkaloids.—Atropine, cinchonidine, diamorphine, morphine, quinidine, quinine, strychnine, and most other alkaloids precipitate insoluble mercurochrome. Caffeine, theobromine sodium salicylate, theophylline sodium acetate, and some others give no precipitate.

Anaesthetics.—Cocaine hydrochloride, ethocaine hydrochloride, alypin, butyn, stovaine, and practically all local anaesthetics precipitate insoluble mercurochrome.

Stains on the skin may be removed by solution of chlorinated soda.

Mercury, Preparations of.

INCOMPATIBILITY.

Grey Powder, which contains chalk, should not be prescribed with acids, or with confection of sulphur, which contains potassium acid tartrate.

Mercury Ointment should not be applied at the same time as sulphur is given internally or applied externally, mercury sulphide being formed in the skin. Iodine or iodides, internally or externally, should also be avoided when mercury is being applied.

Mercury, Ammoniated. 'White Precipitate.'

Used chiefly as ointment, but occasionally as lotion (1 : 20) or dusting powder.

INCOMPATIBILITY.

Alkalis.—Alkali hydroxides (*e.g.*, lime water) liberate ammonia and form a yellow salt.

Iodine.—Forms nitrogen iodide: danger of explosion.

Mercury, Ammoniated (*continued*).

Water.—*Slow* decomposition into ammonium chloride and yellow mercury salt. Lotions should be fresh.

Mercury Oxide. Mercuric Oxide.

Ointments for the eye containing red or yellow mercuric oxide should not be used while iodine is given internally. Severe irritation of the eye has been caused in this way.

Mercury Perchloride. Mercuric Chloride ; Corrosive Sublimate.

Dose.—$\frac{1}{32}$ to $\frac{1}{16}$ grain (0·002 to 0·004 gm.).

Solubility.—Water, 1 : 18 ; alcohol or ether, 1 : 4. The aqueous solution slowly decomposes ; this is prevented by addition of ammonium chloride.

Incompatibility.

Albuminous Fluids.—Precipitates albumin ; this is prevented by sodium or ammonium chloride.

Alkalis.—Alkali hydroxides (*e.g.*, lime water) precipitate mercuric oxide (used in making ' yellow wash '). Ammonia precipitates ammoniated mercury.

Alkaloids.—Precipitates most alkaloidal salts.

Borax.—Precipitate of reddish brown mercuric oxychloride.

Bromides.—Precipitate of white mercuric bromide, soluble in excess of either ingredient.

Iodides.—With potassium iodide, red mercuric iodide is formed, but this is soluble in excess of the iodide, forming a double salt, which is frequently prescribed.

Steel Instruments are readily attacked by the solution.

Sulphur and *Sulphides* form mercuric sulphide.

Tannin and preparations containing tannin are precipitated.

Mercury Subchloride. Mercurous Chloride ; Calomel.

Dose.—$\frac{1}{2}$ to 5 grains (0·03 to 0·3 gm.).

Solubility.—Insoluble in water, alcohol, or ether.

Incompatibility.

Alkalis.—Lime water precipitates black mercurous oxide (used in making ' black wash ').

Bromides.—With potassium bromide and moisture forms mercuric chloride and metallic mercury. Potassium iodide has a similar effect.

Cocaine.—Should not be combined in eye ointments as traces of mercuric chloride are formed and may prove irritating.

Iodine.—Tincture of iodine with calomel precipitates mercuric iodide (used as lotion for ringworm). Iodine and calomel should not be combined in an ointment, which may prove irritating. Potassium iodide should be avoided when calomel is used externally. Iodoform is decomposed by calomel.

Mercury Subchloride (*continued*).

Phenazone forms traces of mercuric chloride, but the amount is negligible.

Sodium Bicarbonate, notwithstanding opinions expressed in certain quarters, is *quite compatible* with calomel.

Sulphur and *Sulphides* form black mercury sulphide.

Methyl Salicylate.

Solubility.—Water, slightly ; alcohol, glacial acetic acid, carbon disulphide, readily.

Incompatibility.—Gives a violet colour with ferric salts, and other reactions of salicylates (*q.v.*). Decomposed by alkali hydroxides.

Morphine and Salts.

Dose.—$\frac{1}{8}$ to $\frac{1}{2}$ grain (0·008 to 0·03 gm.).

Solubility.—In water : acetate 1 : 2·5 ; hydrochloride, 1 : 25 ; tartrate, 1 : 11.

Incompatibility.—In addition to the usual reactions for alkaloids, morphine gives a blue colour, changing to green, with ferric chloride in neutral solution.

Nitroglycerin.

Trinitroglycerin ; Trinitrin ; Glonoin ; Glyceryl Trinitrate.

Dose.—Solution in alcohol, 1 per cent., $\frac{1}{2}$ to 2 minims (0·03 to 0·12 c.c.) gradually increased ; tablets, $\frac{1}{130}$ grain in chocolate, 1 or 2 tablets.

Incompatibility.—Safe in one per cent. alcoholic solution, but dilution liberates an oily substance which is highly explosive. Alkalis decompose nitroglycerin : should the solution be spilled, caustic potash should be poured over it. The chocolate tablets are quite safe. The same remarks apply to *Erythrol Tetranitrate*, which is also explosive.

Oils, Fixed.

The only fixed oils soluble in alcohol are castor oil and croton oil. Fixed oils are *not* soluble in or miscible with glycerin. Alkaline hydroxides form soaps with fixed oils : this is made use of in the preparation of emulsions.

Oils, Mineral.

Liquid paraffin can be emulsified with gum acacia. With castor oil it appears to mix, but the mixture soon separates into layers.

Oils, Volatile.

Most volatile oils are freely soluble in alcohol and only very slightly so in water. Addition of water to an alcoholic solution throws out the oil.

Ointment Bases.

Lard, simple ointment, and soft paraffin will absorb from 12 to 20 per cent. of water; lanolin will take up more than its own weight. Lanolin (hydrous wool-fat) is most readily absorbed by the skin; soft paraffin is least so. The other bases come midway between these.

Lard on exposure to air becomes acid and liberates iodine from potassium iodide.

Paraldehyde.

Dose.—30 to 120 minims (2 to 8 c.c.).

Incompatibility.—Liberates iodine from potassium iodide. Has been known to form an explosive combination with almond mixture.

Pepsin, Pancreatin, etc.

Preparations of the digestive ferments are very liable to be put out of action by other drugs. The action of pepsin is inhibited by alcohol, alkalis, magnesium sulphate, paraldehyde, and some other drugs. Liquid preparations of pepsin invariably contain hydrochloric acid and are therefore incompatible with alkalis.

Phenacetin. Para-acet-phenetidin; Acetphenetedin.

Dose.—5 to 15 grains (0·3 to 1·0 gm.).

Solubility.—Water, practically insoluble; alcohol, 1 : 21. Preferably prescribed in cachets.

Incompatibility.—Forms a pasty mass with salicylic acid, also becomes liquid with chloral hydrate or carbolic acid. Yellow colour with spirit of nitrous ether.

Phenazone. Antipyrin.

Dose.—5 to 15 grains (0·3 to 1·0 gm.).

Solubility.—Freely soluble in water, alcohol, and chloroform.

Incompatibility.

Acetanilide.—Forms a pasty mass.

Calomel.—A small portion of the calomel is converted into corrosive sublimate.

Chloral Hydrate.—Forms a liquid.

Ferric Chloride.—Gives a deep-red colour.

Phenol : *Piperazine.*—Forms a liquid.

Sodium Salicylate.—Dry, forms a pasty mass; in solution, crystals of antipyrin salicylate are said to separate.

Spirit of Nitrous Ether.—Gives a green colour.

Picric Acid. Trinitrophenol; Carbazotic Acid.

Solubility.—Water, 1 : 90; alcohol, 1 : 10. Solutions are intensely yellow and stain the skin. Lotion for burns is one per cent. in water.

Incompatibility.—Must be carefully handled on account of its explosive character. Must not be rubbed or heated with readily oxidizable substances, such as sulphur. Precipitates most alkaloids.

Piperazine. Diethylene-diamine.

Dose.—4 to 10 grains (0·25 to 0·6 gm.).

Solubility.—Readily in water, less so in alcohol. Aqueous solution readily decomposes. Being hygroscopic, it should not be prescribed in powder form.

Incompatibility.

Acetanilide, *Antipyrin.*—Liquid or paste; same with chloral hydrate, phenacetin, carbolic acid, etc.

Alkaloids.—Being strongly alkaline, precipitates most alkaloids.

Iron Salts.—Green or brown precipitate.

Spirit of Nitrous Ether.—Yellow to red coloration.

Potassium Chlorate.

Dose.—5 to 15 grains (0·3 to 1·0 gm.).

Solubility.—Water, 1 : 16; 30 grains to one ounce should be the maximum strength of any solution.

Incompatibility.—Dangerously explosive when mixed with any reducing agent such as sulphur, phosphorus or hypophosphites, sugar, tannin, glycerin, ferrous salts, reduced iron, iodine, etc. (Compound liquorice powder contains sulphur; honey contains sugar.)

Hydrochloric acid added to potassium chlorate evolves chlorine gas; this reaction is employed in making chlorine gargle.

Potassium Iodide.

Dose.—5 to 20 grains (0·3 to 1·2 gm.).

Solubility.—Water, 1 : 1; alcohol, 1 : 12.

Incompatibility.

Acids, *Mineral.*—Iodine is set free.

Alkaloids.—Alkaloid precipitated.

Ammonium Chloride.—Iodine liberated unless mixture is alkaline.

Chloral Hydrate.—In presence of alcohol, an oily layer of chloral alcoholate is formed.

Ferric Chloride Tincture.—Liberates iodine.

Hydrogen Peroxide externally and potassium iodide internally may liberate nascent iodine in the skin, with severe irritation.

Mercury Ointment.—Applied while potassium iodide is given internally may result in irritation from mercuric iodide.

Mercury Perchloride.—*See* Mercury Perchloride.

Mercury Subchloride.—May be partly converted into perchloride.

Paraldehyde.—Iodine is set free.

Spirit of Nitrous Ether.—If the spirit is acid, iodine will be liberated; this may be prevented by previous neutralization of the spirit with potassium carbonate.

Potassium Permanganate.

Dose.—1 to 3 grains (0·06 to 0·2 gm.).

Solubility.—Water, 1 : 20.

Potassium Permanganate (*continued*).

INCOMPATIBILITY.—Potassium permanganate *should never be prescribed with anything except pure water*. It is incompatible with reducing agents and with organic substances of all kinds, and frequently explodes when mixed with these. When ordered in pills no other drug should be added, and the choice of excipient (such as kaolin ointment) should be left to the pharmacist.

Quinine and its Salts.

SOLUBILITY.—Quinine sulphate is practically insoluble in water, but may be rendered soluble by the addition of one minim of dilute sulphuric acid to each grain of the salt. When solution in oils or fats is desired, as in making quinine oleate or ointment, the basic alkaloid only should be used.

INCOMPATIBILITY.—Quinine has all the incompatibilities of alkaloids (*q.v.*); alkalis precipitate the alkaloid, and benzoates, salicylates, and tartrates give a bulky precipitate.

Picric Acid precipitates quinine.

Acetylsalicylic Acid is *not* incompatible with quinine, statements to the contrary notwithstanding.

Resorcin. Resorcinol.

DOSE.—1 to 5 grains (0·06 to 0·3 gm.).

SOLUBILITY.—Freely soluble in water, alcohol, ether, glycerin; soluble in olive oil; slightly soluble in chloroform. Aqueous solution becomes red on exposure to air.

INCOMPATIBILITY.

Alkalis.—Discoloration is hastened in solution.

Quinine Sulphates.—Precipitate.

Spirit of Nitrous Ether.—Red colour.

Resorcin forms a semiliquid mass when triturated with acetanilide, camphor, phenol, menthol, etc.

Roses, Infusion of.

Infusion of roses contains sulphuric acid, which brings out its red colour. It is therefore incompatible with alkalis, excess of which will turn the mixture green.

Salicylates. Salicylic Acid and its salts.

SOLUBILITY.—Salicylic acid is sparingly soluble in water, but fairly soluble (1 : 3·5) in alcohol. Alkalis and borax increase its solubility in water. Alkaline salicylates are very soluble in water; other salicylates as a rule sparingly so.

INCOMPATIBILITY.

Acetanilide.—Forms a paste with salicylic acid.

Acids.—Salicylates are decomposed by mineral acids, salicylic acid being precipitated.

Alkaloids.—Precipitated by salicylates.

Salicylates (*continued*).

Ferric Salts.—Give with salicylates a deep purple colour of ferric salicylate.

Phenacetin.—Forms a paste with salicylic acid.

Spirit of Nitrous Ether.—Salicylates give a yellow to red colour.

Salol. Phenyl Salicylate.

Dose.—5 to 20 grains (0·3 to 1·2 gm.).

Solubility.—Water, almost insoluble; alcohol, 1 : 10; oils, liquid paraffin, fairly soluble.

Incompatibility.—Salol has all the incompatibilities of salicylates, but as it is insoluble in water these apply only to alcoholic solutions. Salol forms a paste with many dry substances, as phenazone, camphor, chloral hydrate, phenol, etc.

Silver Nitrate. Lunar Caustic.

Dose.—$\frac{1}{4}$ to $\frac{1}{2}$ grain (16 to 30 mg.).

Solubility.—Freely in water; sparingly in alcohol. Solutions should be made with distilled water and kept protected from light.

Incompatibility.—Chlorides (as in tap water) precipitate silver chloride; borax and tannic acid also precipitate silver borate and tannate. Carbonates, bromides, iodides, cyanides, citrates, and salicylates also precipitate the corresponding silver salt.

Silver Oxide.

Dose.—$\frac{1}{2}$ to 2 grains (0·03 to 0·12 gm.) in pill.

Solubility.—Insoluble in water.

Incompatibility.—Readily parts with its oxygen, often with explosive violence, when mixed with organic substances, sulphur, phosphorus, etc. Pills should be made with kaolin ointment, like those of potassium permanganate.

Silver, Organic Compounds.

Solubility.—The organic silver compounds as a rule are soluble in water: silver vitellin (argyrol) in all proportions; silver proteinate (protargol), with careful dispensing, 1 : 2.

Incompatibility.

Silver vitellin (argyrol) is incompatible with chlorides, tannic acid, zinc sulphate, and lead acetate, a precipitate being formed in each case. Cocaine hydrochloride precipitates silver chloride: cocaine nitrate should be used. Solutions of argyrol stain the skin: stains may be removed by solution of mercuric chloride.

Silver proteinate (protargol) gives a precipitate with much the same substances as does argyrol, also with alkaloids. Addition of glycerin to the solution makes it very irritating (Robinson). Being an organic substance it is incompatible with potassium permanganate.

Sodium Bicarbonate.—*See* **Alkalis**, *also* **Carbonates.**

Sodium Thiosulphate. Sodium Hyposulphite.

Dose.—10 to 60 grains (0·6 to 4 gm.).

Solubility.—Water, 1 : 1 ; alcohol, insoluble.

Incompatibility.

Acids.—Precipitate sulphur and liberate SO_2.

Oxidizing Substances.—Explosive.

Silver and *Mercury Salts.*—Reduces these to metallic state or to sulphides.

Sodium Salicylate.—*See* **Salicylates.**

Spirit of Nitrous Ether. Sweet Spirit of Nitre.

Dose.—15 to 60 minims (1 to 4 c.c.).

Incompatibility.—Most of the reactions mentioned below take place when the spirit is *acid*, as it usually is. Previous neutralization with potassium carbonate will avoid reactions due to acid.

Acetanilide.—Yellow colour.

Carbonates.—Effervescence.

Iodides and *Bromides.*—Iodine is liberated (*see* Potassium Iodide).

Phenazone.—Green colour.

Resorcin.—Dark red colour.

Salicylates.—Yellow to red colour.

Tannic Acid.—Explosive reaction.

Strophanthus Tincture.

Dose.—2 to 5 minims (0·12 to 0·3 c.c.).

Incompatibility.—When tincture of strophanthus is prescribed in aqueous mixture the glucoside is slowly hydrolysed and the mixture is liable to produce purgation and to lose its effect on the heart (*see* Glucosides).

Strychnine.

Dose.—$\frac{1}{64}$ to $\frac{1}{16}$ grain (1 to 4 mg.).

Solubility.—The alkaloid is practically insoluble in water ; the hydrochloride is soluble, 1 : 60.

Incompatibility.—Strychnine and its salts have all the incompatibilities of alkaloids (*q.v.*). Liquor strychninae hydrochloridi ought not to be prescribed with alkalis or alkaline preparations, such as liquor arsenicalis, unless sufficient water is added to hold the liberated alkaloid in solution (℥i will require at least 10 ounces of water). It is said that sodium *bicarbonate* does not precipitate strychnine as such, but forms a soluble bicarbonate (*Pharm. Jour.*, 1924, Mar. 29, 337, but see p. 15).

Sugar.

The reducing action of sugar should be borne in mind and it should not be prescribed with oxidizing agents. It should be remembered in this connexion that sugar is an ingredient in compound liquorice powder.

Sulphur.

Sulphur is a reducing agent and should not be combined with an oxidizing agent. Sulphur is an ingredient in compound liquorice powder. It forms sulphides with the heavy metals, as lead, mercury, etc. Confection of sulphur contains potassium acid tartrate (acid) and is incompatible with grey powder, which contains chalk. Sulphur is contained in ichthyol (*q.v.*).

Tannic Acid. Tannin.

Dose.—5 to 10 grains (0·3 to 0·6 gm.).

Solubility.—Water, 1 : 1 ; alcohol, 1 : 1 ; glycerin, 1 : 1 slowly.

Incompatibility.—Tannin is contained in most vegetable drugs, and its incompatibilities apply to these also (*see* Infusions).

Albumin.—Tannic acid forms insoluble albumin tannate with all albuminous substances.

Alkaloids.—Precipitates nearly all alkaloids as tannate.

Copper, *Mercury*, *Lead*, *Silver*, *etc.*—Precipitates salts of all the heavy metals.

Glucosides.—Precipitates most glucosides.

Iodine.—Decolorizes liquid iodine preparations.

Iron Salts.—Forms blue-black solution or precipitate with ferric salts.

Phenazone.—Same as alkaloids.

Potassium Permanganate is reduced by tannic acid.

Spirit of Nitrous Ether is decomposed with effervescence.

Thymol.

Dose.—$\frac{1}{2}$ to 2 grains (0·03 to 0·12 gm.) ; as an anthelmintic, 15 to 30 grains (1 to 2 gm.).

Solubility.—Water, almost insoluble ; alcohol, freely ; solution of sodium hydroxide, freely.

Incompatibility.—Forms liquid or semiliquid combinations with acetanilide, camphor, chloral hydrate, menthol, phenazone, phenol, salol, and some other substances.

Zinc Salts.

Incompatibility.

Zinc Chloride is freely soluble in water, but in dilute solutions a flocculent precipitate of hydroxychloride is formed. The solution can be cleared by addition of a few drops of diluted hydrochloric acid.

Zinc Sulphate is incompatible with lead salts, forming insoluble lead sulphate.

Zinc Valerianate is incompatible with acids, valerianic acid being separated.

Soluble zinc salts form insoluble compounds with alkaline hydroxides, carbonates, and phosphates, also with borax.

INDEX

NOTE.—Drugs are indexed under their English names only. Figures in heavy type (*e.g.*, **34**) refer to items in Part II.

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